THE USE OF SOLVENTS
IN SYNTHETIC
ORGANIC CHEMISTRY

BY

DONALD W. MacARDLE, S. B.
ASSISTANT PROFESSOR, BOSTON UNIVERSITY

NEW YORK
D. VAN NOSTRAND COMPANY
Eight Warren Street
1925

Copyright, 1925, by
D. VAN NOSTRAND COMPANY

All rights reserved, including that of translation
into Scandinavian and other foreign languages.

UNIVERSITY OF ARIZONA
LIBRARY

Printed in the U. S. A.

541.346
M11

To

HENRY PAUL TALBOT, PH.D., SC.D.
DEAN OF STUDENTS
THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY

SCIENTIST — TEACHER — FRIEND

55938

PREFACE

This volume is planned as the first part of a treatise on the operative technique of synthetic organic chemistry, similar in a general way to the first sections of the well-known German works of Lassar-Cohn and of Weyl. The author's first intention was merely to translate one or the other of these older works, but the immense amount of revision necessary to change such a book from a fifteen-year-old German treatise to an up-to-date volume for the American chemist made it seem at once easier and more profitable to compile an original work in the same field.

This work is avowedly a compilation; the services of the author have been merely the gathering and arranging of suitable material from chemical journals from all parts of the world. The weaknesses of such a plan are obvious; the author justifies it on the ground that the many investigators whose results have here been included must be more conversant with their various fields and more certain of their various results than any one man could be.

Because of the large number of references and cross-references, the usual plan of citing original sources by the use of footnotes to each page has been abandoned in favor of a single bibliography at the end of the book. In almost every case (with the exception of the most readily available journals) cross-references to abstract journals have been given. The author hopes that this feature will be of service to the chemist who does not have ready access to an extensive journal library.

The author wishes to express his gratitude to Mr. Thomas J. Homer of the Boston Public Library, who was of invaluable assistance in locating the hundred or more journals which were consulted in the preparation of this work; to the Librarian and assistants of the Library of the Massachusetts Institute of Technology, who made freely accessible to the author the resources of that great scientific library; to the Director of the

Boston Public Library and to the other librarians in and near Boston, who by their active co-operation facilitated the collection of much of the material herein contained; to Dr. H. V. Williams, for assistance in translation from the Russian; to Dr. Spencer W. Prentiss and to Dr. Allan Winter Rowe, for suggested changes and additions in the manuscript; to the many chemists who in their correspondence with the author have added material of value; and, most of all, to Dr. Henry P. Talbot, at whose suggestion the preparation of this monograph was undertaken, and who by encouragement and advice has done much to bring the work to completion.

DONALD W. MACARDLE.

BOSTON, *April*, 1925.

CONTENTS

CHAP. PAGE

I. General Considerations 1

II. Inorganic Solvents; Organic Solvents for Inorganic Salts .. 21

III. Alcohols as Solvents 40

IV. The Preparation of Absolute Alcohols 51

V. Higher Alcohols and Ethers as Solvents 74

VI. Organic Acids, Esters, Ketones, and Bases as Solvents 91

VII. Hydrocarbons as Solvents 114

VIII. Inert Liquids as Solvents; Solid Diluents 129

IX. Special Means of Inducing Crystallization 143

X. Salting Out 158

Bibliography 169

Index of Authors 195

Index of Solvents 207

Index of Subjects 209

THE USE OF SOLVENTS IN SYNTHETIC ORGANIC CHEMISTRY

CHAPTER I

GENERAL CONSIDERATIONS

A. Solution

In carrying out any chemical reaction, intimate mixing of the reacting compounds is of prime importance. If the reaction is between gases, little difficulty is found in attaining this end, since all gases are miscible in all proportions; by passing the mixture through a tube filled with glass beads or broken porcelain, almost complete uniformity may be ensured. Generally speaking, however, reactions between gases are of comparatively small importance in organic chemistry, with the exception of the catalytic reduction processes carried out by passing a mixture of hydrogen and the vapor of the compound to be reduced over a heated catalyst. The direct chlorination of methane and ethane has been extensively investigated[1]*, but in the main no great success has been attained because of the explosive character of the reaction which takes place between equivalent quantities of the hydrocarbon and chlorine, producing almost exclusively carbon and hydrogen chloride. To avoid this difficulty, one or the other of the components of the reaction may be used in excess, but the chlorinated products are then difficult to separate because of their dilution. Jones and Allison[2] obtained good results by the direct chlorination of a natural gas consisting almost entirely of methane and ethane; a mixture of this gas and chlorine in practically theoretical proportions was passed over activated charcoal at about 400°.

The original method of Reimer and Tiemann[3] for the synthesis of aromatic aldehydes by the interaction of chloroform, a caustic alkali, and phenol in aqueous solution, was based on the capability which immiscible liquids possess of entering into reaction at their contact surface. This method was of great importance for laboratory use, but was not applicable industrially because of the very low yields, which in some cases did not exceed 5% of theory. The process was materially improved by adding the alkali gradually instead of all at once, but it was only when alcohol was substituted for water as a solvent, as suggested by Traub[4], that side reactions were cut down sufficiently for the method to be of technical value. While the decrease in the reaction temperature due to the lower boiling point of the solvent was of advantage,* the improvement was due chiefly to the greater ease with which the chloroform might react: in other words, to the fact that all the reacting substances were in homogeneous solution.

---

* Superior numbers in all cases refer to bibliography on pp. 169–193.

That complete miscibility is not necessary for reaction is exemplified by methods for the saponification of fats with aqueous alkali, and by a process used industrially for the manufacture of benzoic acid, in which benzyl chloride, a liquid practically insoluble in water, is oxidized by aqueous sodium hypochlorite. In this process the mixture is so vigorously agitated that the benzyl chloride is distributed through the aqueous medium in the form of fine drops; the increase in surface which is brought about in this way is so great that the reaction takes place very rapidly.

Even in the case of liquids sufficiently miscible to permit reaction without undue difficulty, the presence of a solvent is sometimes of advantage; in some reactions involving a liquid, the liquid itself may play the part of solvent. In the preparation of benzyl chloride by the method patented by Loomis[5], chlorine is passed into toluene in the presence of sodium carbonate. In practice the reaction is carried only to about 60% completion (chlorine content in the end product 16–17% instead of 24% as theoretically required for benzyl chloride); the product is then fractionated. The unchanged toluene present serves as a solvent for the reaction, and the chlorinated product is chiefly benzyl chloride, with only small amounts of benzal chloride and ring-substituted products. Should the reaction be continued until

* See page 8.

no unchlorinated toluene remained, the product would be mostly higher chlorinated compounds (benzal chloride, benzotrichloride, and substituted chlorotoluenes) with but little benzyl chloride.

It is in reactions in which one or more of the components is a solid that the use of solvents is most important. Almost any liquid may be, and indeed has been, used as a solvent in some reaction, but in any given case the number of suitable solvents is limited, and generally one liquid possesses distinct advantages over all others. The ends attained by the use of solvents are threefold. First and most important, the reacting substances are brought into a physical condition most conducive to smooth and complete reaction. With ionizing solvents, the dissociation of the solute is perhaps the chief effect, but in non-ionic reactions — and these include the great majority of cases dealt with in organic chemistry — the effect is probably merely that of very fine division and complete mixing. The work of van t'Hoff showed that dissolved substances possess many of the characteristics of gases; it is possible that in most cases the main function of the solvent is merely the holding of the reacting compounds in the state of almost molecular subdivision. The second function of the solvent may be the alteration or improvement of the course of the reaction. Finally, the solvent may influence the rate of reaction, and in that way modify the result. The use of an excess of one of the reacting substances in the simple chlorination of natural gas is a case of this kind, since the substance used in excess is present really as a solvent. In this case the excess gas decreases the rate of combination by absorbing the heat of the exothermic reaction, thus preventing explosive destruction of the apparatus and decomposition of the reacting substances.

Walther and Hübner[6] prepared phenylamino acetonitriles (R.CH(CN)NHR′) by dissolving the corresponding aldehyde and amine in glacial acetic acid and adding potassium cyanide in small portions. They considered that the acetic acid functioned in five ways: (1) as a solvent for the components; (2) as an acid to liberate the hydrocyanic acid from the cyanide; (3) as a suitable solvent to retain the hydrocyanic acid with a minimum of loss; (4) as a medium for the condensation; and (5) as a solvent from which to crystallize the product of the reaction.

Theoretical Aspect of Solution.

True solution does not involve chemical reaction between the solvent and the solute. Thus it is not strictly correct to speak of "dissolving" a solid acid in an aqueous alkali; the alkali neutralizes the acid, and a solution of the resulting salt, not of the acid itself, is obtained. Electrolytic dissociation,* solvation, or molecular association would not invalidate the claim to true solution, since these effects are not strictly speaking chemical reactions, and the solute may be recovered unchanged by removal of the solvent. In their discussion of molecular composition in solution, Noyes and Sherrill[10] remark: "The molecular weights of substances are ordinarily found to be the same in the dissolved state as in the gaseous state; but hydroxyl compounds (such as the alcohols and organic acids) form in non-oxygenated solvents (such as benzene or chloroform) double or even more highly associated molecules. This indicates that the molecules of hydroxyl compounds are associated also in the state of pure liquids. Oxygenated solvents (such as water, alcohols, acetic acid, ether, and acetone) have the power of breaking down these associated molecules into simple ones."

The most generally useful rules of solubility have been summarized by Dehn[11], who quoted from Bigelow[12], Ostromysslensky[13], and Carnelly and Thomson[14] as follows:

(1) Chemically similar substances are usually mutually soluble, and chemically dissimilar substances are usually but slightly soluble in each other[12].

(2) Homologs are mutually soluble[13].

(3) Stereoisomers are mutually soluble[13].

(4) Poly-substituted products (*e.g.*, the four chlorine substitution products of methane) are mutually soluble[13].

(5) The most fusible isomeric substances are the most soluble[14].†

---

* Walden and Centnerszwer[7] tabulated certain physical constants for a considerable number of non-aqueous solvents, and Jacobsohn[8] has discussed in great detail the dissociating powers of inorganic solvents. In an extensive series of papers, Walden[9] discussed organic solvents from the standpoint of their ionizing powers.

†Hildebrand[15] expresses this rule: "A solid having a higher melting-point is" generally "less soluble at a given temperature than one having a lower melting

(6) The most fusible isomeric acids are the most soluble; the solubilities of their salts are in the same order[14].

(7) The order of solubility of isomeric compounds is the same in all solvents[14].

(8) The ratio of solubility of two isomers in any given solvent is nearly constant and is independent of the nature of the solvent[14].

According to McDaniel[16], the solubilities of methane, ethane, and ethylene in various solvents were in the same order, but this order was quite different from that found by Just[17] for the solubilities of nitrogen, hydrogen, carbon dioxide, and carbon monoxide in the same liquids. Just found lower solubility values for hydrocarbon solvents than for alcohols, while McDaniel obtained just the opposite results; aliphatic hydrocarbons were better solvents for the gases which he used than were aromatic hydrocarbons. In addition to bearing out rule (1) cited above, the work of these two investigators indicated that the specific nature of the solute exercised quite as much influence on its solubility as did the nature of the solvent.

Methods of Bringing About Solution.

In most cases no great difficulty is experienced in dissolving a substance in a medium in which it is soluble. Rapid solution is facilitated by (1) fine division of the solid, to give as great a surface as possible; (2) stirring or shaking the solution, so that the solid is constantly brought in contact with fresh solvent; and (3) warming the solution (if no reaction or decomposition is

---

point," and gives the data in the following table as illustration:

Solute	Melting point	Solubility, mole fraction at 25°, in	
		Ether	Benzene
Anthraquinone........	282°	0.00037	0.0013
Anthracene............	217°	0.0059	0.0081
Phenanthrene.........	100°	0.151	0.207
p-Dibromobenzene.....	87°	0.183	0.217
Naphthalene..........	80°	......	0.290

caused thereby), since with very few exceptions* solubilities increase as the temperature is raised. The first of these points is particularly to be observed; crystals should be ground or broken up whenever possible, and with lumpy powdered material it is often profitable to pass the powder through a 20- or 30-mesh sieve.

If a slightly soluble compound is to be submitted to a reaction, sometimes special methods may be used for obtaining the material in a finely divided state, so that the reaction will progress more rapidly and smoothly. For example, in preparing sulfanilic acid (solubility $_{15°}$ 0.89 g./100 cc. water) for diazotization, a slight excess of alkali is added to a suspension of the acid; by acidification free sulfanilic acid is precipitated. In this way a very finely divided product is obtained which is readily acted upon by nitrous acid. Hunn[20] found that 2-nitro-4-chloroaniline was not diazotized even after three hours with an excess of nitrous acid. By dissolving the amine in concentrated sulfuric acid and pouring the solution into water a precipitate was obtained that was so finely divided that ready and complete diazotization with the theoretical amount of nitrous acid was possible.

Bogert and Hand[21] found that bromoacettoluide was very hard to wet again after it had once been dried. It was found necessary to dissolve the toluide in the least possible quantity of boiling acetone, and reprecipitate with a large volume of boiling water. A mud-like mass resulted, which readily entered into reaction. Rule[22] reported that mandeliminohydrin, of which water at 25° dissolved 1.87 g. per 100 cc., could be shaken for five or six days in a shaking machine with an excess of water without dissolving, but at the end of that time the bulk of the hydrin suddenly passed into solution.

---

* As an instance of an exception to this rule, the effect of rising temperature on the solubility of lithium chloride in quinoline, as observed by Walton and Wise[18], may be cited. A solubility maximum was found at 67°; the solubility of the chloride at 96° was little more than a third of the maximum value. An equally curious phenomenon of a somewhat different kind was reported by Deans and Edmonton[19] in connection with an investigation of the method of the British Pharmacopoeia for the determination of the ether-soluble portion of scammony resin. When 10 cc. of solvent were used for two grams of resin, the weight of extracted material was 93.6% of the weight of the sample; with 20 cc. of ether, 77.4% was extracted, and with 30 cc., only 75.3%.

Choice of Solvent.*

The **purity** of the solvent has in some cases a great influence on the solubility of certain compounds. Manning[27] determined the solubility of gallotannic acid in various solvents. One gram of dry ethyl acetate dissolved 0.2 g. of tannin, and 1 g. of dry amyl acetate dissolved 0.1 g.; the addition of 5% by volume of water to the two solvents increased the solubility to 2.5 g. and 0.84 g. respectively per gram of solvent.† He also stated that the solubility of carbohydrates and glucosides in amyl alcohol, acetone, and ethyl acetate was much increased by the addition of a small percentage of water, but not to the extent found for tannin. Oudemans[28] reported that in a mixture of 23% alcohol and 77% chloroform, cinchonine was almost eight times as soluble as in pure alcohol, and more than twenty times as soluble as in pure chloroform. Dehn[11] found that a number of compounds were more soluble in a mixture of pyridine and water, of concentration corresponding to pyridine monohydrate, than in either pure dry pyridine or pure water. The solubilities of helianthine in water, pyridine, and 50% pyridine were determined respectively as 0.02, 0.75, and 62.50.

A striking case of increased solubility in mixed solvents was studied by Gallotti and Giampalmo[29]. They found that zein‡ was entirely insoluble in water, absolute alcohol, chloroform, and acetone; 70% aqueous alcohol, on the other hand, dissolved nearly 20% of zein, and mixtures of chloroform or acetone with aqueous alcohol dissolved the protein freely.

---

* Landau[23] pointed out the marked effect on optical rotation of solutes which was manifested by various solvents possessing active groups (CHO, COOH, etc.) Mosenthal[24] gave a list of several hundred liquids, of the most varied kinds, which had been mentioned in patents as solvents for nitrocellulose, and further data of this kind were given by Mehren[25]. Dimroth and Bamberger[26] discussed the effect of various solvents on the stability of organic molecular compounds.

† It may be noted that, contrary to statements frequently found in reference books concerning the solubility of gallotannic acid, this compound is very soluble in water, even at low temperatures. Manning found that at 0° a saturated aqueous solution of his carefully purified tannin was a perfectly clear, brownish syrup containing less than 1.5 g. water to 1 g. tannin. In the commercial preparation of technical tannic acid, syrups of about the consistency of molasses, and containing 60% or more tannic acid, are regularly handled.

‡ A protein from corn described by Chittenden and Osborne[30].

An example of the opposite solubility effect, *i.e.*, the repression of solubility by the presence of a trace of impurity in the solvent, was given by Marden and Dover[31]. Lithium chloride is insoluble in benzene at 25°, but is soluble 1.78 g./100 cc. in ethyl acetate. The addition of 1% of benzene to a saturated solution of the salt in ethyl acetate precipitated about 20% of the lithium chloride in solution. By increasing the benzene content of the solution to 10%, the solubility of the chloride was reduced from 1.78% to 0.147%.

A slight modification in a reaction sometimes calls for a change of solvents. By oxidation of equal molecular proportions of 1,8-naphthalene diamine and *o*-amino dimethyl-*p*-toluidine, a dyestuff was formed[32]. If the diamine or its salts were soluble in water, as in the case given, the reaction proceeded satisfactorily. This was not the case with tolyl-1,8-naphthalene diamine, but when phenol was used as solvent instead of water[33], good results were obtained.

Other physical characteristics besides its power of solution should be considered in the choice of a solvent. This is particularly true of the **boiling-point.** If a reaction takes place best at a certain (elevated) temperature, it will be most satisfactory to use when possible a solvent which boils at about the desired reaction temperature; the reaction may then be carried out under a reflux condenser without the necessity of further precautions of temperature regulation. The availability of such a procedure is of course limited by the possibility of some abnormal effect of the chosen solvent on the course of the reaction. Thus, it was to increase the convenience of their procedure that Schenck and Römer[34] used tetrachloroethane (b. 135°) as solvent for the treatment of phosphorus pentachloride with ammonium chloride. The optimum reaction temperature was 130–140°, and work in sealed tubes or autoclaves was unsatisfactory because of the evolution of hydrogen chloride as a reaction product. By the use of tetrachloroethane, the reaction could be carried out in open vessels under the most favorable conditions.

Löb[35] found that when nitrobenzene and metallic sodium were boiled together in benzene solution, there was little reduction of the nitrobenzene. The surface of the metal soon became covered with a brown coating which hindered further reaction, even on long boiling. On the other hand, when boiling toluene was used, a very vigorous reaction took place. This difference in effect was due probably to the fact that sodium (m. 97°) melts in boiling toluene (b. 111°) but not in boiling benzene (b. 80°). Toluene was used as solvent by Kyrides[36] in the preparation of triphenylguanidine. The reaction appeared to proceed best at about 110° (the boiling point of toluene), the raw materials — aniline and thiocarbanilide — and the end-product triphenylguanidine dissolved freely in the boiling toluene, and pure product crystallized as the toluene cooled. The marked advantage of this solvent was that the water formed in the reaction distilled with the toluene vapors, so that by use of a condenser, a separator, and a return-flow pipe the reaction might be carried on in a solvent which was at all times substantially anhydrous.

Renshaw and Holm[37] prepared trimethyl arsine by the interaction of zinc methyl and arsenious chloride in ether, in which solvent both compounds readily dissolved. When the reaction was completed, much difficulty was experienced in separating the mixture of trimethyl arsine (b. 52°) and ether (b. 35°) by fractional distillation. When xylene (b. 140°) was used as a reaction medium, the yield of pure product was several times as large as before, and its boiling-point range, with fewer distillations, was much smaller.

Aside from the effects of its physical properties, the solvent may alter either the **reaction product** or the **yield.** Hayduck[38], by brominating phenanthrene in carbon disulfide solution, obtained phenanthrene dibromide as the main product, with small amounts of the mono- and dibromo derivatives, while Zetter[39], by using ether as a solvent, obtained bromo derivatives only. Palkin[40] found that the alkaline condensation of a quinoline derivative in chloroform gave cyanine with but small traces of dicyanine, but that condensation in alcohol which contained a little chloroform gave far better yields of dicyanine than were obtained with pure alcohol as solvent.

In the course of their investigations of the ammonium salts of organic acids, Bateman and Conrad[41] found that when weak acids were under investigation, the ammonium salts could be satisfactorily prepared by passing ammonia into an alcoholic solution of the acid, but that when using this method for strong acids, like dichloro- and trichloroacetic acid, a considerable amount of the acid esterified with the solvent alcohol. The ammonia seemed to act as a condensing agent, and the esterification was facilitated by the heat generated by the neutralization of the acid by the ammonia. A similar effect was noted by McMaster[42] for hydrocinnamic acid, and by McMaster and Magill[43] for glycollic acid.

Guareschi[44] prepared benzyl alcohol by the reduction of benzamid with sodium amalgam, using ether saturated with water as a solvent. West[45] substituted 95% alcohol for the moist ether, and found that the yield was thereby increased from 31.5% of theoretical to 56%. Friedburg and Mandel[46] obtained good results by using a solution of nitrogen trioxide in carbon disulfide as a reagent for the preparation of pure nitroso compounds; this solution was slowly added to a carbon disulfide solution of the substance to be acted upon. Since benzoic acid was very slightly soluble in carbon disulfide, ethyl alcohol was used as solvent for this acid; nitrosobenzoic acid was formed in fairly good yield, but there was also formed a considerable quantity of nitrous ether and of ethyl benzoate. Olivier[47] noted that *p*-chlorophenyl sulfone chloride in ethereal solution, when exposed to air and direct sunlight or ultraviolet light, decomposed to a considerable extent (35–40%) with the evolution of chlorine and formation of *p*-chlorophenyl sulfonic acid. The same effect was noted, but to a much smaller degree, in chloroform solution, but not at all in carbon tetrachloride, carbon disulfide, benzene, or turpentine.

The solvent may also have a fundamental effect on the **velocity** of a reaction.* Menschutkin[48] determined the speed of the reaction between *n*-triethyl amine and ethyl iodide in more than twenty inert solvents. The velocity constant was found to vary from 0.000180 (hexane) to 0.133 (benzyl alcohol): a ratio of 742 to 1. No law to cover the various cases could be laid down. Similar work was done by Patterson and Montgomerie[49], who measured the velocity with which anis*syn*aldoxime in various inert solvents changed to the *anti* form. The results of other workers in this field were summarized, and it was pointed out that the data obtained by very different processes varying greatly in type, showed some remarkable regularities. This would indicate that the effect of the solvent on reaction velocity was to some extent a specific property of the solvent. Hawkins[50] showed that variation which he observed in the rate of the reaction between pyridine and allyl bromide was not due to complex formation; the velocity of this reaction was about fifty times as great in nitrobenzene solution as in toluene. Carleton[51] studied the rate of reaction between finely comminuted sodium and *iso*amyl bromide in various solvents, by determining the amount of sodium bromide formed. When dimethylaniline was used as the solvent, the reaction was complete in a few hours. With ether, four days were required, and in benzene solution the reaction after two weeks was only 10% complete. Carleton suggested that in dimethylaniline solution it was probable that a salt (dimethyl-*iso*amyl-phenylammonium bromide) was formed by interaction of solvent and solute, and that the sodium reacted with this salt as a positive metal replacing a less positive radical. Arnall[52] found that by a suitable choice of solvents the nitration of phenol could be made to go almost instantaneously (with acetic anhydride as solvent) or so slowly that it would be only 55% complete after 48 hours (absolute alcohol as solvent).*

---

* The name **adjuvance** has been applied by Dr. Spencer W. Prentiss of the Massachusetts Institute of Technology to this characteristic property of solvents.

Interliquefaction.†

The liquefaction of two solid compounds, or a solid and a gas, when intimately mixed, is a phenomenon of more interest than usefulness. One of the first instances noted of this unusual effect was mentioned in a paper by Brown[61], who found that if equal parts of chloral hydrate and camphor or menthol were rubbed together, a thick oil was formed which could not be made to crystallize. The mutual effect of these compounds was also remarked some years later by Schär[62]. Wallach[63] reported that the two isomeric oximes of amylene nitrosate formed good crystals when pure, but that if crystals of these isomers were rubbed together, an oil resulted which did not crystallize even on standing for months.

---

* For further investigations of the effect of solvents on reaction velocity, see the work of Menschutkin[53], Carrara[54], von Hemptinne and Bekaert[55], Sagrebin[56], Brühl[57], Dimroth[58], Tubandt[59], Cohen[60], and others.

† The phenomenon here described has been noted by a number of authors, but in no case does any name seem to have been assigned to it. The name here used, proposed by Dr. Austin M. Patterson in reply to an inquiry by the writer regarding the accepted name, was considered by several authorities on nomenclature to whom it was submitted, as the best of several possible names suggested.

Dunlap[64] observed that when molecular quantities of sodium acetate and *o*-toluidine hydrochloride were intimately ground in a mortar, the mass became first moist and pasty, and finally semifluid. Perhaps the only careful investigation of interliquefaction is that carried out by Moore[65], who found that piperonal (m. 37°) liquefied when exposed to dry hydrogen chloride under pressures greater than about 500 mm. When the pressure of the hydrogen chloride was reduced, gas was evolved from the liquid; crystals appeared, and within a few minutes the liquid solidified into a mass of crystals of piperonal of the proper melting point.* A possible explanation of the interliquefaction of two solids is that it is a case of melting-point lowering similar to that shown by the majority of mixtures of two crystalline organic compounds† and that the result is comparable to the melting of ice by salt, but such an explanation can hardly be applied to the system: piperonal-hydrogen chloride.

B. Crystallization

The chief and in most cases the only purpose of crystallization is the purification of the compound sought, taking advantage of the fact that the impurities present are, under suitable temperature conditions, either more soluble or less soluble in the solvent used than is the desired compound. Only in rare instances is the obtaining of large crystals an end in itself, and in such work the use of special methods of crystallization is generally necessary. In the course of an investigation of some of the electrical properties of crystals, carried out by Moore[67], it became necessary to procure large pieces of wholly clear Rochelle salt crystals. Perfect crystals up to three inches in length were obtained by very slowly and carefully cooling a saturated solution of the salt. To produce a clear, perfectly developed crystal of the size stated required a period of about one month, during which time the rate of cooling was at first only about 0.1° per day, and at the end not more than 0.5–0.6° per day.

---

* In a private communication Dr. Moore informed the writer that he had often observed the interliquefaction of two solids in the preparation of Schiff's bases with such mixtures as piperonal and *p*-toluidine. Liquefaction occurred and the temperature fell; then came chemical reaction, water separation and consequent cloudiness, rise of temperature, and solidification of the Schiff's base.

† An interesting discussion of the distinction between solution and fusion, dealing with phenomena similar to those mentioned in this section, may be found in a paper by Bancroft[66].

Since the rate of cooling is the chief factor in the formation of large crystals, it is sometimes possible to obtain good-sized crystals by slow cooling under ordinary laboratory conditions. To do this, the beaker containing the hot saturated solution is immersed in a large volume of water at the same temperature; because of increased heat content this system will cool more slowly than would the saturated solution alone. Jannasch and Bartels[68] found that by crystallizing hexaethylbenzene from alcohol in this way they could obtain crystals 10–20 cm. in length. The cooling may be still further retarded by lagging the large container with asbestos or with a towel; excellent results might be expected from the use of a "fireless cooker" in this procedure.

In the great majority of cases, however, the end attained by the crystallization of solids is similar to that sought in the fractional distillation of liquids or of liquefied gases.* The solid material to be purified may be contaminated with iron filings, dirt, or bits of filter paper, and may contain solid by-products or tar. The operations incident to the removal of these impurities is beyond the scope of the present discussion; the first point to consider is the choice of solvent.

Choice of Solvent.

Crystallization consists in saturating a solvent with a (generally) impure solute, and by change of temperature or other means, causing the solute to separate in a more nearly pure condition, and in a crystalline form. The most readily available means for decreasing the solubility is that of cooling the solution. For this reason the solvent chosen should be one which at higher temperatures freely dissolves the compound sought, and in which the solubility rapidly decreases as the temperature falls; sometimes after filtering off the first and purest crop of crystals it may be desirable to obtain a second crop by cooling the mother liquor of the first in ice water (if water is the solvent) or in a freezing mixture (if a low-melting solvent like alcohol or ether is used). It is desirable that the solvent chosen should be one in which the temperature-solubility coefficient of the impurities present differs as widely as possible from that of the substance sought, since the object of the crystallization is to retain in the mother liquor one of the components — generally the impurity — while the other separates. It is desirable also that the material be sufficiently soluble in the hot solvent to allow the crystallization to be carried out with conveniently small volumes of liquid.

---

* Regarding the latter, see the work of Burrell *et al*[69].

Hildebrand[70] discussed the choice of solvent for recrystallizations from the standpoint of polarity and internal pressure.* When the substance to be purified is of low melting-point, it will be very soluble in liquids having similar internal pressure and polarity. Hence it is better to select a solvent different from the solute in one or the other of these factors, so as to produce a smaller solubility. This has the advantage of giving a larger temperature coefficient of solubility. For example, a paraffin of melting-point below 100° would be most soluble (in terms of mole fraction) in liquids like hexane, silicon tetrachloride, and mesitylene, and its solubility, already being a maximum so far as the choice of solvent is concerned, would not increase so rapidly with temperature as would its solubility in a liquid like ethylene bromide, from which it differs in internal pressure, or in a liquid like alcohol, where the deviation would be due to a difference in polarity. Hence, in cooling from, say, 50° to 20°, a greater portion of the paraffin would separate from its solutions in ethylene bromide or alcohol than from solutions in hexane. Moreover, in this case the impurities present would likely be substances of higher internal pressure than the paraffin, such as unsaturated bodies, which would remain in the mother liquor more readily if the solvent were one of higher internal pressure or polarity. Where a substance of high melting point or low solubility, like anthracene, is being recrystallized, it may be desirable to use a solvent of similar internal pressure in order to secure larger solubility than would be possible in a liquid of very different internal pressure or of high polarity.

---

* For further consideration of this aspect of solubility, see the work of Hildebrand[71], Mortimer[72], and others.

If the compound dealt with is volatile in the vapor of the solvent, proper precautions must be taken to avoid loss. Thus, if benzoic acid is to be crystallized from water, the solution should not be heated above 70–80°. An instance of this came under the observation of the writer some years ago. In the crystallization of benzoic acid on a plant scale the temperature of the solution was allowed to rise to about 95°; the resulting fumes made work for a time impossible, and coated all parts of the unit with benzoic acid crystals. A similar instance was pointed out by Haworth and Perkin[73] in connection with the preparation of ethylene glycol by hydrolysis of ethylene bromide. In the standard procedure, the aqueous reaction solution was evaporated and the glycol extracted from the concentrated solution; in this method a great part of the glycol was lost because of its volatility with steam. This source of loss was obviated by carrying out the reaction under a reflux condenser until the solution was very strong in glycol, and then distilling off the excess water, which was condensed and used as solvent for the next batch.

If possible the solvent chosen should be one which may readily be evaporated from the purified crystals; sometimes special precautions regarding this point must be taken. Orndorff and Hitch[74] reported that tetrachlorofluorescein carbinolcarboxylic acid was partially dehydrated to red tetrachlorofluorescein on recrystallization from methyl alcohol, ethyl alcohol, or ether, when the excess of solvent was distilled off at atmospheric pressure, or when the solutions were allowed to evaporate spontaneously. They found, however, that a pure product could be obtained by crystallization from absolute ethyl alcohol, if the excess of solvent was distilled off under reduced pressure at a temperature not exceeding 35°. It may here be pointed out that if a compound is crystallized from a high-boiling solvent (**A**), and is for purposes of ready drying washed with another solvent (**B**) of lower boiling point, the crystals should first be washed with a mixture of solvents **A** and **B**, as the addition of **B** to crystals to which the mother liquor of **A** adheres may precipitate impurities soluble in **A** but insoluble in **B**. Wieland and Rheinheimer[75] prepared phenarsazine by boiling its methyl ether in methyldiphenylamine. The crystals of phenarsazine which separated on cooling were filtered from the mother liquor, washed with a mixture of equal parts of methyldiphenylamine and benzene, then with pure benzene, and finally with ether.

An instance of the benefit of a proper choice of solvents is found in a simple method used by the writer some years ago for preparing for organic chlorine determination samples of moist benzoic acid contaminated with sodium chloride. Crystallization from water was precluded by the possible loss in the mother liquor of the trace of chlorine-containing organic compound, and by the inconvenience and the time limitations. Absolute alcohol dissolves only small quantities of sodium chloride, but even traces of salt would invalidate the analysis, as the chlorine sought was less than 0.1%. Benzene was found to be an ideal solvent for this purpose: a few grams of the wet sample were dissolved in about 50 cc. of benzene, the inorganic salts and water filtered off, and the benzene solution of benzoic acid evaporated at a low temperature. This method took a minimum of time, and blank analyses showed complete removal of inorganic salts. A similar method was used by Benedict[76] for purifying wet technical picric acid, and by Ullman and Nádai[77] for purifying technical *p*-tolyl sulfonic chloride. Three hundred grams of the crude material were dissolved in 300 cc. benzene, the separated water drawn off, and the solution filtered. About half of the benzene was distilled off, and on addition of ligroin the chloride separated as a white crystal meal, which was dried in the air. The work of Clark[78] on the purification of anthracene, carbazole, and phenanthrene furnishes an excellent example of a difficult separation carried out by the proper use of a number of different solvents.

Another point to be considered in selecting a solvent for a crystallization is the possibility of chemical action between the solvent and the solute. For example, Jackson and Robinson[79] reported that if bromodinitrophenylacetic acid was recrystallized five times from alcohol, it was entirely converted to bromodinitrotoluene. Water also caused the same decomposition, although not so rapidly, but the compound could be crystallized from very dilute sulfuric acid without decomposition.

Wislicenus and Erbe[80] showed that the crystal form of formylphenylacetanilide depended on the solvent from which it was crystallized. The α (labile) form was obtained when benzene or petroleum ether was used, and the β (stabile) form from ether, acetone, or glacial acetic acid. Either form could be changed to the other by crystallizing from the proper solvent.

Solvent of Crystallization.

In inorganic salts the presence of water of crystallization is not uncommon. The same is true with organic compounds, and not only water, but alcohol, phenol, and many other solvents form loose molecular compounds with solutes crystallized from them. Norris[81] pointed out that certain derivatives of tetraphenyl ethylene and of triphenylmethane formed molecular compounds with the following solvents: carbon tetrachloride, chloroform, carbon tetrabromide, bromoform, chlorodibromomethane, acetone, methylethyl ketone, diethyl ketone, and sulfuryl chloride.* Triphenyl carbinol seemed to take 0.75 moles of carbon tetrachloride of crystallization.

The empirical formulas of such compounds are not always readily determined. Some compounds retain their solvent of crystallization with surprising tenacity, while others cause difficulty in an accurate determination of formulas because of their efflorescence. Schöpff[82] reported that barium acridone sulfonate lost the last of its 1.5 moles of crystal water only at 220°. An instance of the uncertainty caused by efflorescence is given by Latschinoff[83], who found that choleic acid ($C_{24}H_{40}O_4$)† apparently crystallized with 6.40% of water. One and a half moles of water would give a loss of 6.24% on drying, but it seemed more probable that the crystals formed with two molecules of water to each molecule of acid, and lost a part of this during the low-temperature drying which was necessary to remove surface moisture. Similarly, 7.5% of acetone was found after crystallization from that solvent, instead of 12.5% as calculated for the one molecule which probably was originally present; when crystallized from glacial acetic acid and dried over caustic potash until no odor of acetic acid was distinguishable, the crystals contained 9.7% of solvent, while 1 mole of solvent of crystallization would show a loss of 12.9%.

---

* See also page 124.

† Lassar-Cohn[84] showed that this is the true formula for choleic acid, instead of $C_{25}H_{42}O_4$ as given by Latschinoff.

McKee and Berkheiser[85] studied the effect of light on the velocity of efflorescence of sulfanilic acid, which ordinarily, when freshly prepared, contains two molecules of water. Samples of the crystals were placed in two tubes, stoppered with absorbent cotton, one of which was wrapped with lightproof paper; both tubes were exposed to direct sunlight for ten days. The sample which had been directly exposed lost 98% of its water in that time, while the sample protected by the lightproof paper lost but 35%, though the temperature in the second tube was nearly 3° higher than in the first.

According to Posternak[86] the calcium-sodium salt of inisitohexaphosphoric acid had a formula $C_6H_6O_{24}P_6Ca_2Na_8 + nH_2O$, in which n might be 33, 23, 8, 3, 1, or 0, depending on the temperature and the humidity of the air to which the salt had been exposed. Sometimes various solvents unite with a given compound in entirely different molecular proportions. Schmidlin and Massini[87] found that trinaphthyl carbinol separated from ether and from benzene in crystals of the compositions $2R.3Et_2O$ and $3R.C_6H_6$ respectively; the molecular ratio of the two solvents in the crystals was accordingly $9Et_2O$ to $2C_6H_6$.

According to Büchner and Witter[88], when an aqueous solution of hydrated citric acid (this acid crystallizes both with and without water of crystallization) was partially evaporated at a temperature of 130° and was then left to cool, crystals of the anhydrous modification were obtained, in spite of the presence of water. If the product was recrystallized, even from cold water, the anhydrous form continued to separate, unless the solution was inoculated with a crystal of the hydrated acid. The lead salts from the anhydrous acid were also anhydrous, while those prepared from the hydrated modification separated with water of crystallization. Behr[89] observed that in the same way grape sugar might be crystallized in either the anhydrous or the hydrated form by the use of the corresponding seed crystals, and pointed out that the possibility of separation of anhydrous crystals from a dilute solution of grape sugar might be due to the fact that crystals of this modification are not deliquescent, so that they would be stable when once formed. McKee and Berkheiser[85] found that while sulfanilic acid, crystallized from water at ordinary temperatures, contained two molecules of water, if the crystallization was carried out above 80° the crystals were almost anhydrous.

Wyrouboff[90] reported that cinchonidine hydrobromide crystallized from water with $\frac{2}{3}H_2O$, and from alcohol in crystals apparently having the formula $B.HBr.\frac{1}{3}H_2O.\frac{1}{4}EtOH$. He suggested the possibility that the crystals were actually an equimolecular mixture of the salt with $\frac{2}{3}H_2O$ and that with $\frac{1}{2}EtOH$, but was unable to isolate the latter salt. Lassar-Cohn[91] remarked that the salt with $\frac{3}{8}EtOH$ would give almost exactly the loss on heating that was actually observed, and considered this the most probable formula, since Wyrouboff made no mention of tests applied to prove that there was actually water present in the crystals. The existence of a complex formula similar to that proposed by Wyrouboff would not, however, be unique; de Bruyn[92] showed definitely that the hydrated sulfates of nickel and of magnesium, when crystallized from methyl alcohol, gave crystals of the formula $MSO_4.3H_2O.3MeOH$, and Hesse[93] found that conchairamine, an alkaloid of the quinine group, separated from alcohol in crystals of the formula $C_{22}H_{26}N_2O_4.H_2O.EtOH$. Marsh[94] found that the double iodides of mercury and the alkali metals separated from aqueous methyl carbonate in crystals of the formula $MHgI_3.H_2O.nMe_2CO_3$, in which n was 1, 2, or 3.

Mixed Crystals.

Not only do many chemical compounds take solvent of crystallization, but in some cases two solid compounds give more or less stable homogeneous crystals. As early as 1839 Calloud and Brunner[95] observed that the sugar obtained by the hydrolysis of starch crystallized with a definite proportion of sodium chloride, which could not be removed by repeated crystallizations. Fischer and Schmidmer[96] prepared an addition product ($2C_6H_{12}O_6$ + NaCl) probably identical with this by dissolving the calculated weights of salt and grape sugar in the minimum amount of water, evaporating to a syrup, and adding methyl alcohol. The crystals were purified by dissolving in a little water and precipitating again with alcohol. Kolbe and Lautemann[97] found that benzoic and cinnamic acids formed mixed crystals in the molecular ratio of 2 : 1. Herrmann[98] described the formation of mixed crystals of two acids which, when pure, crystallized in different crystallographic systems, but Hantzsch and Herrmann[99] were not able to duplicate this result when using an isomer of one of the acids in conjunction with the other. Chemical similarity in some cases promotes the formation of mixed crystals: Hlasiwetz and Barth[100] obtained crystals containing equal molecular amounts of *p*-hydroxybenzoic acid and protocatechuic acid (3,4-dihydroxybenzoic acid), and Cohn[101] reported a similar result when working with *p*-nitrobenzoic acid and *p*-acetylamino benzoic acid.

CHAPTER II

INORGANIC SOLVENTS; ORGANIC SOLVENTS FOR INORGANIC SALTS

Water.

In organic as well as in inorganic processes, water is by far the most generally-used solvent. Aside from the availability and cheapness of water, its solvent powers for inorganic substances far exceed those of any other liquid, and for organic compounds only alcohol is superior. The dissociating power of water renders it the natural solvent for ionic reactions. There are also the advantages of inertness, non-flammability, and, except in rare instances, absence of need for special purification.

Because of the importance of purification methods involving the extraction of aqueous solutions with immiscible organic solvents, various investigators have made determinations of the mutual solubility of water and certain of the more common non-aqueous solvents. Some of these results are given in table I on the following page.

Only in rare instances is it necessary to use water purified in so careful a manner as that required by Harvey[110] in his work on the photogenic compounds present in the firefly. Distilled water, which was used in a specially devised apparatus, was freed from oxygen by admitting hydrogen which had been passed over glowing platinum to remove oxygen. By alternate bubblings and evacuations the dissolved oxygen was soon removed. The same end may be attained, to a degree sufficiently complete for most purposes, by bubbling carbon dioxide or illuminating gas through the water.

Crystallization from water may be of peculiar advantage owing to the solubility in water of some impurity present in the crude material dealt with. Datta and Gupto[111] found that 2,6-dichlorodihydroxy-3,5-dichloro-4-ketoheptane decomposed with evolution of hydrogen chloride, but retained sufficient of the gas to

TABLE I

MUTUAL SOLUBILITIES OF WATER AND SOME NON-AQUEOUS SOLVENTS*

A	B	Grams of solute in 100 g. saturated solution at 20-25°	
		A in B	B in A
chloroform	water	0.643 (H)	0.099 (H) 0.084 (C)
carbon disulfide	"	0.225 (H)	0.744 (H) 0.010 (C)
ether	"	5.15 (H) 6.89 (F & C)	3.83 (H) 1.10 (F & C) 1.3 (W & F)
benzene	"	0.072 (H)	0.240 (H) 0.061 (G) 0.046 (C)
amyl alcohol	"	2.62 (H)	2.62 (H) (*iso*) 9.8 (W, N&W)
ligroin (sp. gr. 0.665)	"	0.227 (H)	0.516 (H)
ligroin (sp. gr. 0.70)	"		0.097 (C)
kerosene (sp. gr. 0.792)	"		0.073 (C)
paraffin oil (sp. gr. 0.883)	"		0.047 (C)

REFERENCES

H = Herz[102]
C = Clifford[103]
W & F = Wade and Finnemore[104]
F & C = Forbes and Coolidge[105]
G = Groschuff[106]
W = Wilson[107]
N & W = Noyes and Westbrook[108]

prevent accurate analysis of the product. A quantity of the oil which had been kept for some time was repeatedly washed with water to remove hydrogen chloride, and was then left under water for some days to crystallize. Analysis showed that the crystals of 3,5-dichloro-2,4,6-triketoheptane were practically free from hydrogen chloride. Clarke and Jones[112] took advantage of the hydrate-forming power of water to obtain pure pinacone from the reduction product of acetone. The mixture was fractionated, and the portion distilling between 150° and 180° was mixed with water and boiled; pinacone hydrate $C_6H_{14}O_2.6H_2O$ separated on cooling, and was purified by recrystallization from water. Fischer and Jaeger[113] studied the solvent action of superheated water (at temperatures ranging up to 300° C.) on phenols and coal-tar hydrocarbons. It was found possible to separate phenols from " carbolic oil " by fractional extraction with superheated water.

---

* See also Fühner[109].

Aqueous Solutions of Inorganic Salts as Solvents; "Hydrotropy."

The solvent power of water for a particular substance may under some circumstances be improved by substituting for pure water an aqueous solution of some inorganic salt. The ability of concentrated solutions of certain salts to dissolve cellulose is well known. Deming[114] mentioned $SbCl_3$, $SnCl_2$, and $ZnBr_2$ in this connection, and stated that solutions of these salts and many others in hydrohalide acids dissolved cellulose with great ease, as did a few salts in formic and acetic acid. If these solutions were poured into water, the cellulose was precipitated, but since it had apparently undergone chemical change, these cases do not come within the limits of the accurate definition of " solution." Palm[115] found that borax solution was useful in extracting certain natural dyestuffs, but it is probable that the alkalinity of the borax solution was the chief merit of this solvent over pure water; the method developed by Wollenberg and Bigelow[116] for purifying crude trinitrotoluene by agitating the finely divided material with a cold 5–10% solution of sodium sulfite is also probably based on some chemical reaction of the solvent. Schunck and Roemer[117] observed that the best method for freeing purpurin from small quantities of alizarin was by repeated crystallizations from alum solution, in which alizarin was only slightly soluble. After most of the alizarin had been removed in this way, pure purpurin was obtained from the partially purified crystals by crystallization from aqueous alcohol.

By " hydrotropy " is meant the characteristic of certain substances to make possible a clear aqueous solution of compounds not soluble in pure water. Substances of this class are of some technical importance (*e.g.*, turkey-red oil to prepare aqueous solutions of fats, and various assistants which give water-soluble cresols for medicinal use) but there has been almost no study of hydrotropic action from a theoretical standpoint. Neuberg[118] pointed out that hydrotropic action was shown by salts of benzoic acid and its substituted derivatives, phenols, soaps, naphthalene sulfonic acids, and many other compounds. By the use of suitable hydrotropic assistants, clear solutions could be prepared of aromatic alcohols, terpenes, fats, alkaloids, carbohydrates, proteins, etc. Witt[119] observed that aqueous solutions of naphthalene sulfonic acids possessed " an astounding capacity for dissolving all manner of substances which are quite insoluble in pure water "; among these soluble substances were the resinous by-products of sulfonation, and the calcium sulfate which was formed in neutralizing the sulfonation mixture.

The hydrotropic power of " turkey-red oil " (the sodium salt of sulfonated castor oil) was utilized by Nottbrack[120] in obtaining aqueous solutions of certain dyestuffs which were not readily soluble in water. Acid or alkali could not be used to bring about solution, as the neutrality of the solution would thereby be destroyed, and alcohol or glycerol would tend to alter the color. Nottbrack used a solution of 20 cc. of 70% oil made up to 100 cc., to which sufficient caustic was added to form a clear neutral liquid. The amount of this assistant necessary to bring about solution depended on the dyestuff and the concentration desired.

The solvent action of soap solutions for oils was used by Link[121] in a process proposed for the purification of naphthalene. The crude material was agitated at 85° with soap solution until nearly dissolved; the crystals which separated on slow cooling of this solution were centrifuged, washed and distilled, giving almost pure naphthalene.

A novel method for the purification of phenylhydrazine was developed by Otto[122]. This compound, slightly soluble in water and virtually insoluble in alkaline solutions, was found to be very soluble in solutions of sodium naphthyl sulfinate; by extraction of such a solution with ether, the phenylhydrazine was obtained pure and crystalline, with a melting point of 23°.

Heuter[123] summarized some of the technical applications of hydrotropy. Dietze[124] described a process for the use of soaps in preparing a stable emulsion of water and benzine or chloroform for defatting leather or textile fibres.*

Hydrogen Peroxide.

Investigations of the solvent powers of hydrogen peroxide have apparently been but limited in number. This compound may readily be prepared in a state of great purity by the distillation method of Maass and Hatcher[129]. Bamberger and Nussbaum[130] studied the solvent properties of highly concentrated or practically anhydrous hydrogen peroxide. They found that concentrated peroxide possessed solvent powers far greater than those of the dilute material commonly at hand. Polyhydroxy compounds and certain proteins were readily dissolved, the solvent action increasing with the concentration of the solvent. Cellulose was very soluble in concentrated peroxide; if the peroxide was too dilute the cellulose swelled without completely dissolving. If the cellulose solution was allowed to stand, a slow reaction took place, with formation of hydrolysis products of cellulose. With some solutes a marked depolymerizing action was shown: paraldehyde dissolved almost completely in peroxide, giving a solution with an intense odor of formaldehyde. Maass and Hatcher and Bamberger and Nussbaum agreed that the explosive tendencies of concentrated hydrogen peroxide have been exaggerated; nevertheless, the former recommended that care be used in its handling, and the latter stated that certain inorganic catalysts, such as iron, lead, and manganese, caused rapid decomposition, and that some organic solutes formed with peroxide vigorously explosive mixtures. In another paper dealing with the solvent properties of peroxide, Maass and Hatcher[131] demonstrated that, contrary to a prevailing impression, the mutual solubility of ether and hydrogen peroxide was slight.*

---

* For other uses of organic alkali salts as assistants for solution, see the work of Rappenstrauch[125], von Heyden[126], Ritsert[127], and various German patents[128].

Inorganic Acids.

The use of inorganic acids as solvents is in many cases adopted because of some chemical action which they exert, or, in the case of concentrated sulfuric acid, the strong affinity of this compound for water. It is for this latter reason that sulfuric acid is so widely used as a solvent in nitrations, since the water formed in the reaction of nitration $R.H + HONO_2 \rightarrow R.NO_2 + H_2O$ is removed from the sphere of action by the concentrated or fuming sulfuric acid, and thus is prevented from diluting the nitric acid.

---

* For determinations of the partition coefficient of hydrogen peroxide between water and various organic solvents, see the work of Walton and Lewis[132] and of Calvert[133].

Halochromy, the property possessed by concentrated sulfuric acid of dissolving dyestuffs to give solutions whose colors are quite different both from the color of the powdered dye and of its aqueous solution, may be due to the dehydrating power of the acid, or to the formation of oxonium salts, but on this subject nothing definite is known, in spite of much speculation. This property is, however, of great service both in identifying dyestuffs and in determining whether a given sample is a single dye or a mixture. In the case of azo-dyestuffs[134], the colors are the same as those formed by the action of concentrated sulfuric acid on the azo-hydrocarbon which is the base of the dyestuff. Thus, azobenzene $C_6H_5N : NC_6H_5$ dissolves in concentrated sulfuric acid to give a brownish-yellow solution, and the same coloration is produced by the action of concentrated acid on both amidoazobenzene $C_6H_5N : NC_6H_4NH_2$ and hydroxyazobenzene $C_6H_5N : NC_6H_4OH$. Practically all dyes give characteristic colors in concentrated sulfuric acid, and often characteristic changes of color as the solution is diluted with water; lists of such colors are given — as properties of the various dyes — in the dyestuff tables of Schultz[135] and of Green[136]. Cain and Thorpe[137] give the following procedure for determining the character — homogeneous or otherwise — of any commercial dyestuff specimen. Two or three drops of concentrated sulfuric acid are placed in a white porcelain dish, and the finely powdered specimen is dusted into it. This can best be effected by placing a small quantity of the dyestuff on the end of a spatula and blowing it on the acid from some little distance away. Notice is then taken as to whether each particle dissolves with the same or a different color. Moir[138] carried out investigations whereby he was able to predict the colors of many organic compounds in sulfuric acid solution.

The separation of *iso*quinoline from quinoline as carried out by Weissgerber[139] is an example of the use of **sulfuric acid** as a solvent because of its acidity. Coal tar quinoline contains a small amount of *iso*quinoline; the separation of this compound may be facilitated by taking advantage of its greater basicity. When the technical material, dissolved in benzene, was shaken with 1/6 the calculated amount of 20% sulfuric acid, the mixture of bases obtained from the sulfates was distinctly richer in *iso*quinoline than was the original material. The method of Harris and Pope[140] for isolating this compound was also based on fractional extraction of the stronger base, though the details of procedure were quite different. Oyster and Adkins[141] removed resins from crude phenanthraquinone by suspending the product in concentrated sulfuric acid for twelve hours. The solution was then diluted to decrease the solubility of the phenanthraquinone, and the precipitate was filtered off. The solvent effect of sulfuric acid on phenanthraquinone, and the increase in solubility as the concentration of the acid was increased, were attributed by Knox and Will[142] to a supposed basic tendency of the quinone to form an unstable sulfate. Vesely and Votocek[143] found that concentrated sulfuric acid extracted all of the basic impurities of anthracene (even compounds as slightly basic as carbazole) from a solution of the crude material in an inert solvent immiscible with the acid; dilute acid extracted only strongly basic impurities like acridine.

Many compounds, particularly aromatic sulfonic acids, possess solubilities in sulfuric acid quite different from their solubilities in water. Ewan and Young[144] prepared nitroguanidine by the rearrangement of guanidine nitrate in 92–98% sulfuric acid, and dilution of the reaction mixture before filtration. The final concentration was decided upon by determining the solubility of the nitro compound in 1 g. of sulfuric acid diluted with varying amounts of water. The solubility per cubic centimeter of dilute acid decreased with diminution of the acid content, but since the amount of acid to be present was predetermined, the optimum dilution was that in which the minimum solubility per gram of concentrated acid was found; in this case the concentration determined was 20%.

The solubility of ether in concentrated sulfuric acid was utilized by Riedel[145] in the purification of ethyl bromide. Ethyl bromide produced by the action of a bromide on ethyl sulfuric acid contained 7–8% ether, which could not be removed by fractionation because of the slight difference of the boiling points (EtBr b. 39°; Et_2O b. 35°). For some uses of the bromide, ether was a very undesirable impurity: in the preparation of nitrophenetol by ethylation of sodium nitrophenolate, the yield was greatly decreased by the presence of ether in the ethyl bromide. If the impure bromide was shaken with portions of concentrated sulfuric acid until the acid formed the lower layer — the dissolved ether at first greatly decreased the specific gravity of the acid — the ether was entirely removed, and the specific gravity of the bromide increased from 1.375–80 to 1.476. Dox and Yoder[146] also used sulfuric acid as solvent in an extraction. In the preparation of dibromopentane from benzoylpiperidine, they obtained a reaction mixture containing dibromopentane and benzonitrile. The latter was completely removed by shaking three or four times in the cold with concentrated sulfuric acid. The brominated hydrocarbon was washed with dilute sodium carbonate, dried, and distilled.

Lonnies[147] crystallized *s*-sulfo *iso*phthalic acid from dilute sulfuric acid, while Heine[148], who tried to crystallize the compound from water, had obtained only a thick syrup. An instance of the opposite effect was noted by Baeyer[149], who crystallized chlorohydurilic acid by dissolving it in concentrated sulfuric acid, and then diluting the solution with water, in which chlorohydurilic acid is insoluble. Vender[150] recommended sulfuric acid as a solvent for crystallizing trinitrotoluene. Concentrated acid at 100° dissolved about its own weight of trinitrotoluene; on cooling, or dilution and cooling, the desired solute crystallized without appreciable loss, while the impurities present (dinitrotoluene, resins, etc.) remained dissolved. Carbazole may likewise be purified by solution in concentrated sulfuric acid and dilution. According to Kirby[151], dilution in the ordinary manner gives a precipitate so fine that it is hard to handle; moreover, the heat of dilution may cause sulfonation of the carbazole. He suggested that the solution be spread in thin layers and exposed to moist air, or that moist air be bubbled through the solution; there will then be nearly complete precipitation of the carbazole in a form which may easily be filtered.

Jackson and Lamar[152] reported that the solubility of dichlorodinitrophenylacetic acid in water was greatly increased by the addition of a small amount of sulfuric acid, although neither hydrochloric nor nitric acids showed such an effect. Dilute sulfuric acid was also the best solvent for bromodinitrophenylacetic acid[79], while pure water caused slow decomposition into bromodinitrotoluene. If a solution of the bromoacetic acid was steam distilled for a few hours, it entirely passed over as the corresponding toluene, but if two or three drops of dilute sulfuric acid were added to the solution, the decomposition was entirely prevented.

Stenhouse and Groves[153] used concentrated sulfuric acid as a solvent for nitrogen trioxide in the preparation of nitrosoörcin. For the electrochemical oxidation of azobenzene to polyhydroxy azobenzenes, Fichter and Jaeck[154] found that the use of 89–95% sulfuric acid as an electrolyzing medium was necessary if good yields of crystallizable oxidation products were to be obtained. The use of dilute (70–80%) acid, which possessed the advantage of much greater conductivity, led to marked decomposition of the azobenzene with the formation of tarry products. The authors stated that the use of concentrated sulfuric acid in the electrochemical oxidation of organic compounds was unusual, since in many cases it would lead to sulfonation and resinification, but in the reaction under consideration the use of this solvent was necessary, as otherwise the oxidation would take place at the azo group instead of in the rings. Fichter and Grisard[155] used 0.5-normal sulfuric acid for the electrolysis of benzonitrile.

As with almost every other solvent, the presence of a trace of impurity in sulfuric acid used as a solvent may occasionally have an effect out of all proportion to the small amount of the impurity present. In preliminary experiments on the action of fuming sulfuric acid containing dissolved sulfur on diamino derivatives of diphenylamine, Battegay and Hugel[156] observed that the solution assumed a deep violet color with red fluorescence. When the experiment was repeated, using another lot of reagents, the color was not obtained until a little of the acid used in the first trial was added. Investigation showed that the color formation was due to traces of selenium in the acid, the colored compound being probably a selenopyronine.

Although the strong nitrating and oxidizing powers of **nitric acid** preclude its general use as a solvent, this acid has occasionally served as a medium from which to crystallize nitro compounds. Brady and Williams[157] used hot nitric acid (sp. gr. 1.4) as a solvent for the first crystallization of crude 3,4-dinitrotoluene, in order to destroy the tarry matter which was present. Will[158] crystallized tetranitronaphthalene by dissolving the material in concentrated nitric acid and precipitating by dilution with water.

The **halogen acids** have also been used in certain cases as solvents. Johnson and Hill[159] crystallized the hydrochloride of 3-nitrotyrosine from concentrated hydrochloric acid, and Schlieper[160] found that this was the only solvent from which he was able to crystallize crude *s*-bromonitrophenol, since when other solvents were used only an oil could be obtained. A similar method was used by Blom[161] for removing resinous impurities from *p*-nitrophenol which had been prepared by the action of potassium ethylate on *p*-chloronitrobenzene. Bogert and Mandelbaum[162] purified thio-*p*-toluidine hydrochloride by dissolving in hot 10% hydrochloric acid, and adding to this solution hot concentrated hydrochloric acid until precipitation began. As the solution cooled, pale yellowish needles of the hydrochloride separated. In order to bring wood or cotton cellulose into solution, Sherrard and Froehlke[163] found it necessary to use 40% hydrochloric acid as solvent. This was prepared by passing hydrogen chloride into ordinary concentrated hydrochloric acid cooled to −10°. Laar[164] reported that while sulfanilic acid which had been crystallized from water at ordinary temperatures contained two molecules of water, an anhydrous modification could be obtained by crystallizing from concentrated hydrochloric acid.

Wales[165] stated that solubility determinations of naphthylamine salts of naphthalene sulfonic acids could not be carried out in pure water as a solvent because of the rapid hydrolysis of the more soluble compounds. An 0.01-N solution of hydrochloric acid was sufficient to prevent hydrolysis in all but one case; no effect of acid of that strength on the solubility could be detected. Fischer[166] found that the solubility of sodium-β-naphthalene sulfonate was about 7% greater in 1-normal hydrochloric acid than in pure water, but that as the acid concentration was further increased, the solubility fell away sharply.

Lenz[167] prepared *p*-fluorobenzene sulfonic acid by diazotizing sulfanilic acid and recrystallizing the diazo compound from warm concentrated **hydrofluoric** acid. Lowy and Dunbrook[168] observed that when *bis*-aniline tellurium tetrabromide was recrystallized twice from dilute **hydrobromic** acid, the base formed a new complex, consisting of four moles of aniline hydrobromide combined with one mole of tellurium tetrabromide. Constant-boiling hydrobromic acid (48% HBr) was used by Bigelow[169] to minimize the hydrolysis of *o*-toluidine diazonium bromide in the preparation of *o*-bromotoluene by the Gattermann reaction.

An interesting use of concentrated hydrochloric acid for separating organic and inorganic compounds was made by Quick[170] in a study of the preparation of *p*-phenylene diamine by heating together dichlorobenzene and ammonia in the presence of a copper salt. The most satisfactory method for separating the diamine was based on the fact that the diamine hydrochloride was insoluble in concentrated hydrochloric acid, whereas ammonium chloride, the copper salt used as catalyst, and almost all other impurities which were present were soluble. The method of procedure was in general as follows: the reaction mixture was filtered to remove unchanged dichlorobenzene and other solid impurities, and the ammonia was driven off with a current of steam. The solution which remained was cooled and filtered, and hydrogen chloride was passed in. As saturation was approached, crystals separated, and soon filled the container. These were filtered off and dried; they were usually of reddish color and were difficult to decolorize, but analysis showed them to be fairly pure, even without recrystallization.

Bogert and Mandelbaum[171] used aqueous solutions of several acids of differing ionization constants as extraction solvents in their work on the preparation of thiotoluidine. The reaction mixture, which had been dissolved in benzene, contained *p*-toluidine, thiotoluidine, and dithiotoluidine; the basicity of these compounds decreased in the order named. By extraction of the benzene solution with 15% aqueous citric acid solution ($k = 0.00081$) practically all the *p*-toluidine was extracted, with only traces of thiotoluidine. The benzene layer was next extracted with a saturated aqueous solution of oxalic acid ($k = 0.10$), which removed the thiotoluidine; the weakly basic dithiotoluidine was finally extracted with 10% sulfuric acid.

Liquefied Gases.*

The solvent properties of liquid ammonia and liquid sulfur dioxide have been but little investigated, due to the low boiling points of these liquids (−38.5° and −10° respectively, at atmospheric pressure) and to the irritating gases which they evolve on vaporization. Franklin and Kraus[173] pointed out the marked similarity as solvents of water and **liquid ammonia,** and determined[174] the solubility in liquid ammonia — generally at atmospheric pressure (−38.5°) — of about 200 inorganic and 250 organic compounds; this work was a continuation of the work reported by Gore[175]. The alkali chlorides were insoluble and the chlorides of the heavy metals readily soluble. Bromides were more soluble than chlorides, and iodides still more soluble. Most of the other salts tested were insoluble. Paraffin hydrocarbons were very slightly soluble or insoluble; higher polyhydroxy alcohols, as erythrite and mannite, were slightly soluble; higher fatty acids and dibasic acids were insoluble. Benzene was 10% soluble, toluene slightly soluble, higher homologues insoluble; aromatic halogen derivatives were slightly soluble; terpenes were insoluble. All other organic compounds dealt with (probably 85% of the number tested) were readily soluble in liquid ammonia or miscible in all proportions with it; the latter was particularly apt to be the case with compounds of low molecular weight. In sealed tubes at 25°, most of the compounds insoluble at atmospheric pressure dissolved readily; the only case observed of reaction between solvent and solute was the formation of ammonium phthalate from phthalic acid at 25°. The work of Bartow and McFarland[176] showed that with some compounds liquid ammonia was much more reactive. Of 42 esters, nine gave amides when dissolved in liquid ammonia, nine gave other alteration products, and the rest were unchanged; acid chlorides for the most part reacts with the solvent to form amides.

In an investigation of certain properties of " ammono-carbonic acids " (guanidine, cyanamide, and similar compounds), Franklin[177] pointed out that compounds which give a very low hydrogen-ion concentration when dissolved in ionizing solvents, are not recognizable as acids in aqueous solution because of the relatively high degree of ionization of water itself into hydrogen and hydroxyl ions. The very much lower degree of auto-ionization which characterizes liquid ammonia as compared with water, permits the manifestation of acid properties by compounds which as acids are much too weak to be recognized as such in aqueous solution. Thus, by the interaction of liquid ammonia solutions of the ammono-carbonic acids and metallic amides, metallic salts of the acids were readily prepared; these salts would of course be incapable of preparation in aqueous solution because of hydrolysis. Franklin and Stafford[178] used liquid ammonia as a solvent for the preparation from potassium amide of potassium salts of acid amides.

---

* For special methods used in the manipulation of small quantities of volatile solvents, see papers by Stock[172].

Kraus and White[179] and White[180] found that the action of sodium on organic compounds in liquid ammonia solution resulted in reduction and side reactions. White[181] found that sodium in liquid ammonia reacted very violently with aryl halides, but that when the solution was diluted with petroleum ether the reaction could readily be controlled. The action of sodium on organic halogen-containing compounds in liquid ammonia has been studied as an analytical method for halogen by Chablay[182], Dains *et al*[183], Clifford[184], and Dains and Brewster[185]. Kraus and Greer[186] reduced trimethyl stannic chloride to trimethyl stannane with sodium, using liquid ammonia as a reaction medium. The solution was placed in a Dewar flask, and agitated during the reaction by a current of gaseous ammonia.

One of the few attempts at the industrial application of liquid ammonia as a solvent was made by Wilton[187], who observed that liquid ammonia under pressure seemed to exert a selective solvent action on the ordinary impurities of crude anthracene. He stated that if the material was powdered and stirred with ammonia under nine atmospheres pressure (about 25°), and the mixture filtered, the filter cake consisted of nearly pure anthracene.

In a process for desulfurizing oils, Clancy[188] made use of the solubility of mineral oils and their distillates, of alkali or alkaline earth metals, and of ammonium persulfate in liquid anhydrous ammonia. By dissolving nitrates of cellulose in liquid ammonia, mixing this solution with any of a large number of organic liquids, and allowing the ammonia to evaporate, Clancy[189] was able to prepare clear solutions of higher nitrates of cellulose in menstrua in which these compounds had previously been thought to be insoluble.

Probably the most extensive investigation of the solvent properties of **liquid sulfur dioxide** was that carried out by Walden[190]. He found that a great variety of compounds were soluble, often with characteristic colors, and he tabulated the solubilities and colors of solution of about eighty compounds, including salts (inorganic and organic), hydrocarbons, alcohols, acids, esters, and bases. Sulfur dioxide is an ionizing solvent, and in some cases the degree of ionization is greater than in aqueous solution. Metathetical reactions between organic compounds and inorganic salts were readily carried out, owing to the fact that, with the exception of alkali iodides, the majority of inorganic salts (including metallic salts of organic acids) were insoluble. Thus trimethyl ammonium chloride and potassium iodide, both of which were soluble, reacted with the precipitation of potassium chloride and the formation of trimethyl ammonium iodide; α-bromo*iso*butyric acid, treated in solution with potassium iodide, gave a precipitate of the potassium salt of the acid and left hydriodic acid in solution. Color reactions, like the thiocyanate test for ferric iron or the ferric chloride test for salicylic acid, might be carried out in liquid sulfur dioxide solution. Walden obtained consistent results in determinations of the molecular weights of some organic compounds by the boiling-point method when liquid sulfur dioxide was used as the solvent.

Grob and Adams[191] proposed the use of liquid sulfur dioxide as a solvent for the sulfonation reaction between sulfur trioxide and aromatic hydrocarbons. By diluting the sulfur trioxide with liquid sulfur dioxide, the action of the former could be made less vigorous and the reaction more easy to control. The presence of sulfur dioxide, a strong reducing agent, lessened oxidation. Finally, since the dehydrating action was minimized by using sulfur dioxide instead of sulfuric acid as a solvent, less decomposition and sulfone formation were encountered. The sulfur dioxide solution of sulfur trioxide was prepared by distilling the trioxide from oleum into a cooled, evacuated vessel, and adding liquid sulfur dioxide. The reaction was allowed to take place for several hours under pressure, after which the sulfur dioxide was distilled back into the first chamber and the sulfonation product and excess sulfur trioxide were left as a residue in the reaction vessel.

Schmitt[192] recommended a mixture of equal parts of acetone and sulfur dioxide as a solvent which possessed all the advantages of liquid sulfur dioxide, but which was much more convenient to work with since temperatures below 0° were not necessary. The use of sulfur dioxide in this form for extracting hydrocarbons from coal and for removing unsaturated hydrocarbons from naphtha has been patented by Plauson[193], who pointed out that while acetone at the temperature of the ice-salt bath would dissolve twice its weight of sulfur dioxide, higher ketones possessed a sufficiently greater solvent power for the gas to permit the use of the ketone-sulfur dioxide mixture in open vessels at room temperature.

Moore *et al*[194] used liquid sulfur dioxide to obtain paraffin hydrocarbons from light petroleum distillate. Benzene and its homologues, and olefines were found to be miscible in all proportions, while pure paraffin hydrocarbons were insoluble. The presence of a high proportion of soluble constituents in the mixture increased the solubility of the paraffins; *e.g.*, a mixture of 50% benzene and 50% paraffins (pentane and hexane) was completely soluble. For mixtures low in soluble constituents the separation was fairly good. The usefulness of sulfur dioxide in this type of work was extended by Krieble and Seyer[195] to the purification of heavy hydrocarbon distillates from sand tar oils. The main difficulty encountered — the viscosity of the heavy hydrocarbons at −10° — was overcome by dissolving the oil in petroleum ether which had previously been treated to remove unsaturated compounds. It was observed that sulfur compounds could be removed by this method, as oils which contained almost 1% of sulfur before this treatment contained only a trace afterwards. Edeleanu[196] carried out an extensive investigation of the applicability of liquid sulfur dioxide in oil refining. Sufficiently favorable results were obtained to warrant the designing of a plant-scale installation.

McKee and Cable[197] described a process by which resinous woods like yellow pine and Douglas fir might be used for sulfite pulp manufacture by extracting the resins with liquid sulfur dioxide; this process was patented by McKee and Holmes[198]. The authors pointed out the fact that liquid sulfur dioxide, costing less than one cent a pound, is by far the cheapest solvent for oils and resins, and is quite devoid of fire risk.

Liquid sulfur dioxide, as well as liquid ammonia, has been used for the purification of crude anthracene[199]. If material containing 30% anthracene was agitated with an equal weight of liquid sulfur dioxide and filtered, about half went into solution, and the crystals remaining had a purity of about 50%; the residue from the evaporation of the filtrate contained not more than 2% anthracene. By using four parts of the solvent, a product of 70–80% purity could be obtained without greatly increasing the loss. Such a purification, it was stated, may be carried out in the laboratory without undue inconvenience, since the spontaneous evaporation of the solvent cools the mixture to such an extent that its vapor pressure is kept fairly low.

While **liquid hydrogen chloride** and **hydrogen bromide** have been carefully studied by Archibald[200] as ionizing solvents for alcohols and organic acids, there has been little investigation of the general solvent characteristics of these liquids. Archibald[201] found that the greater number of alcohols, both aliphatic and aromatic, were soluble in liquid hydrogen bromide. Results which he brought forth later[202] indicated that most aromatic acids and most lower aliphatic acids (except formic acid and saturated polybasic acids) are soluble in liquid hydrogen bromide and in liquid hydrogen chloride; the latter liquid seemed to be the better solvent. Maass and McIntosh[203] indicated the solubilities of a number of organic compounds in these solvents. Steele *et al*[204] reported that in these media very few inorganic substances were soluble, but that a large number of organic compounds — hydrocarbons, alcohols, esters, aldehydes, ketones, cyanides, and nitro compounds — dissolved readily. Archibald and McIntosh[205] and Maass and McIntosh[206] observed that liquid hydrogen chloride, bromide, and iodide formed unstable crystalline addition products with ether, acetone, and ethyl alcohol;

these compounds were further investigated by McIntosh[207], who obtained similar addition products with simple aliphatic acids and esters.

The solvent powers of **liquid carbon dioxide** were investigated by Büchner[208], who confirmed the results of Gore[209] in reporting that inorganic salts were entirely insoluble in this solvent, even at room temperature. A number of organic liquids were miscible in all proportions with liquid carbon dioxide; the solubility of solid organic compounds was in general fairly high, and was dependent to a marked extent upon the temperature.

Little study has been given to **liquid hydrogen sulfide** as a solvent for organic compounds. In an investigation of the ionizing power of this solvent, Antony and Magri[210] found that hydrocarbons, alcohols, nitro derivatives, and many other organic compounds dissolved readily; the solutions were very inactive, and in only a few cases was there reaction between solvent and solute. Similar results were obtained by Walker *et al*[211] and by Quam[212]; the latter worker reported that reactions between solvent and solute seemed most likely to occur when a double-bonded oxygen or a tervalent nitrogen was present in the solute molecule.

Other Inorganic Solvents.

In a paper on the properties of **selenium oxychloride,** Lenher[213] discussed briefly the solvent powers of this liquid for certain organic compounds. Benzene, toluene, chloroform, carbon tetrachloride, and carbon disulfide were miscible in all proportions with the oxychloride; these mixtures might be separated by fractional distillation or by hydrolysis of the oxychloride. Saturated aliphatic hydrocarbons were entirely immiscible with selenium oxychloride, while the unsaturated hydrocarbons united directly with the solvent, often with great violence. It was thus possible to separate such unsaturated hydrocarbons as amylene from heptane by simple contact with selenium oxychloride. Proteins such as silk and leather were dissolved in the cold by this solvent, but cellulose, starch, and sugar were not appreciably acted upon; solutions in selenium oxychloride might be filtered through ordinary filter paper. Vegetable and fish oils reacted as with sulfur monochloride, forming rubber-like masses. Rubber and phenolic condensation products like bakelite dissolved, and chemical change took place. Gums, resins, celluloid, and glues dissolved readily in the cold. The properties of selenium oxybromide[214] resemble in general those of the oxychloride.

In a paper on non-aqueous liquids, Jacobsohn[215] summarized the solvent powers for organic compounds of more than thirty inorganic solvents. He considered ammonia the most general in its solvent action, which for organic compounds was "far greater than water"; next in order of solvent power were SO_2, PCl_3, PBr_3, $POCl_3$, $AsCl_3$, and $AsBr_3$. Hydrogen sulfide, HCl, HBr, HI, and N_2O_4 dissolved "numerous compounds," and HCN, CN, and S_2Cl_2 also manifested a certain degree of solvent action. Quaternary ammonium compounds were found to be soluble in a particularly wide range of inorganic liquids.

ORGANIC SOLVENTS FOR INORGANIC SALTS

The solvent power of various organic liquids (other than alcohols) for inorganic salts has been noted in several isolated instances, but the determination of a number of such solubilities as a problem in itself seems to have been taken up by only a few experimenters. The most general investigation of this subject is perhaps that of von Laszczynski[216], who worked with seven organic solvents and fifteen or more inorganic salts. Among other determinations which he reported, the following may be noted (solubilities are in grams per hundred grams of solvent; the determinations were at room temperature unless otherwise stated). Mercuric chloride was fairly soluble in ether (6.4), more so in ethyl acetate (30.0), and very soluble in acetone (126). Stannous chloride ($SnCl_2.2\ H_2O$) was quite soluble in ether (11.4); boiling ethyl acetate dissolved 73.3 parts of the salt. Potassium thiocyanate was fairly soluble in pyridine (6.1) and in acetone (20.7); the solubility of this salt decreased with rise in temperature (6.7 at 0°; 3.2 at 115°). It is interesting to note that boiling pyridine dissolved 8.6 parts of silver iodide. The solubilities of mercuric halides have also been studied by other workers[217], and Seidenberg[218] investigated the separation of fatty acids as their lead salts by the use of organic solvents.

Krug and McElroy[219] tested in a qualitative or semiquantitative manner the solubilities in acetone of about sixty salts; among the few qualitative values which they gave was one for the solubility of mercuric chloride (60 g. per 100 g. acetone at 25°) quite different from that found by von Laszczynsky. Similar information was obtained by Naumann[220] for acetone[221], ethyl acetate[222], pyridine[223], methyl acetate[224], acetonitrile[225], and benzonitrile[226], by Bourgom[227] for methylal, by Eidmann[228] for acetone and for methylal, and by Stuckgold[229] for ethyl urethane. Sachs[230] recommended the use of acetone as a solvent for oxidations with permanganate of compounds insoluble in water, since acetone at 20° dissolves 2.4% of permanganate, and at 40°, 4%; the oxidation products may in many cases be precipitated by diluting the solution with water. Pyridine may also be used as a stable solvent for permanganate oxidations. In 1859 St. Gilles[231] had reported that acetone dissolved potassium permanganate without being affected, even at the boiling point.

Hill[232] observed that the solubility of silver perchlorate in benzene was greatly increased by the presence of small amounts of water. Benzene saturated with water, containing less than 0.25% of water by weight, dissolved more than twice the amount of salt that could be dissolved in perfectly dry benzene. The solubility of silver perchlorate in water, it may be observed, is exceptionally high (540 g. salt per 100 g. water at 25°).

CHAPTER III

ALCOHOLS AS SOLVENTS

Solvent Powers for Inorganic Compounds.

Since methyl and ethyl alcohols are by far the most important organic solvents, it is not surprising that they should have received careful study as solvents for inorganic substances. Work on this subject was carried out in great detail by de Bruyn[233], who collected and correlated solubility data obtained by other investigators, and by further experimental work established generalizations which greatly simplify the consideration of the solvent properties of methyl and ethyl alcohols. He was able to lay down the general rule, tested with particular care for inorganic compounds, that all substances, with a single exception (sulfur), are more soluble in methyl alcohol than in ethyl alcohol. Among inorganic salts this difference (see table II, p. 41) might be slight ($AgNO_3$) or very marked ($BaBr_2$); sugars were only slightly soluble in methyl alcohol, but were practically insoluble in ethyl. Ammonia, sulfur dioxide, and hydrogen chloride followed the rule, though it may be noted that a solution of the last-named gas in methyl alcohol lost strength by esterification about twenty times as rapidly as in ethyl alcohol. Of the two sodium alcoholates, the methylate was more soluble in the corresponding alcohol than was the ethylate, and the solution was more stable, but sodium ethylate was the better reducing agent. The rule formulated by Dumas and Peligot[240] that methyl alcohol, as regards its solvent power, stands intermediate between water and ethyl alcohol, was thus borne out for compounds most soluble in water — this group included practically all salts, and carbohydrates, urea, and ammonia — but hydrogen chloride, sulfur dioxide, and most organic compounds the solubility of which in water was not great, were more soluble in methyl alcohol than in either water or ethyl alcohol.

TABLE II

SOLUBILITIES OF CERTAIN INORGANIC COMPOUNDS IN ALCOHOLS

All determinations at room temperature unless otherwise stated; expressed in grams per 100 g. solvent. The solubility values for water as a solvent are those given by Seidell[234], and are approximate only.*

Salt	Water	MeOH	EtOH	PrOH†	*iso*-AmOH
LiCl‡	81.5	42.36 (TB)	25.83 (TB)	16.22 (TB)	9.03 (TB)
LiI	167.	343.4 (TB)	250.8 (TB)	47.52 (TB)	112.5 (TB)
NaCl	36.	1.31 (TB)	0.065 (TB)	0.012 (TB)	0.002 (TB)
		1.41 (B)	0.065 (B)		
NaBr	31.	17.2 (B)			
		18.5 (HK)	3.58 (HK)	0.92 (HK)	
NaI	184.	90.35 (TB)	46.02 (TB)	28.22 (TB)	16.30 (TB)
		77.7 (B)	43.1 (B)		
		91.3 (HK)	48.2 (HK)	31.9 (HK)	
$NaNO_2$	34.	4.43 (B)	0.31 (B)		
$NaNO_3$	90.	0.41 (B)	0.036 (B)		
KCl	35.5	0.53 (TB)	0.022 (TB)	0.004 (TB)	0.0008 (TB)
		0.5 (B)	0.034 (B)		
KBr	67.5	2.17 (TB)	0.142 (TB)	0.035 (TB)	0.003 (TB)
		1.51 (B)	0.13 (B)		
KI§	148.	18.04 (TB)	2.16 (TB)	0.43 (TB)	0.098 (TB)
		16.5 (B)	1.75 (B)		
		17.1 (HK)	1.97 (HK)	0.54 (HK)	
KCN	....	4.91 (B)	0.88 (B)		
RbCl	91.	1.41 (TB)	0.078 (TB)	0.015 (TB)	0.0025 (TB)
NH_4Cl	39.	3.35 (B)	0.62 (B)		
		3.54 (HK)	0.68 (HK)	0.23 (HK)	
NH_4Br	75.5	12.5 (B)	3.22 (B)		
		12.9 (HK)	3.26 (HK	1.19 (HK)	
NH_4NO_3	214.	17.1 (B)	3.8 (B)		
$NH_2OH.HCl$	....	16.4 (B)	4.3 (B)		
$CuCl_2$	28.	68.0 (B)	53.4 (B)		
$CuSO_4$	22.5	1.05 (B)			
$AgNO_3$	257.	3.72 (B)	3.1 (B)		
$HgCl_2$	7.	66.9 (B)	49.5 (B)		
		65.9 (HK)	50.0 (HK)	26.0 (HK)	
$HgBr_2$	0.6	69.5 (HK)	30.4 (HK)	17.6 (HK)	
HgI_2	0.005	4.03 (HK)	2.29 (HK)	1.77 (HK)	
$Hg(CN)_2$	11.5	44.2 (B)	10.1 (B)		
		46.9 (HK)	10.6 (HK)	4.28 (HK)	
$BaCl_2$	37.	2.18 (B)			
$BaBr_2$	106.	50.0 (B)	2.8 (B)		
NH_3 (0°)	87.5	41.5 (B)	24.5 (B)		
NH_3 (28°)	41.	17.4 (B)	10.1 (B)		
SO_2 (0°)	23.	247.0 (B)	115.0 (B)		
SO_2 (26°)	9.5	47.0 (B)	32.3 (B)		
HCl (0°)	82.5	105.0 (B)	83.0 (B)		
HCl (32°)	65.5	75.1 (B)	61.6 (B)		
Cl_2 (0°)	1.5	27. (B)	reacts		
Cl_2(−11.5°)	....	42. (B)	reacts		

REFERENCES: TB = Turner and Bissett[235]
B = de Bruyn[236]
HK = Herz and Kuhn[237] (data recalculated).

For notes see page 42.

As with water, the solubilities in both alcohols of sodium salts were greater than those of the corresponding potassium salts. Similarly, iodides were more soluble than bromides, and bromides than chlorides; the single exception noted to this rule was that mercuric chloride was more soluble in alcohols than mercuric iodide, and the same was true when water was the solvent. Methyl alcohol was less readily oxidized by permanganate than was ethyl alcohol, and was also much more stable towards the halogens. A slow reaction took place between chlorine and methyl alcohol, while ethyl alcohol was rapidly attacked. A solution of bromine in the latter solvent immediately caused an odor of aldehyde, while in methyl alcohol a solution originally containing 61.7% of bromine showed 57% remaining unchanged after seventy-eight days. Iodine acted slowly on ethyl alcohol, and apparently not at all on methyl alcohol.

A very thorough investigation of the solubilities of the alkali halides in alcohols was carried out by Turner and Bissett[235], and certain regularities in solubility were observed. Except in the case of lithium iodide, the solubility decreased with increasing molecular weight of the solvent; in the two instances which deviated from the rule (when water or propyl alcohol were the solvents), the solution was in equilibrium with a solid phase consisting of hydrate or alcoholate instead of anhydrous salt as was the case with the other three solvents for lithium iodide. In all cases the solubilities increased in the order: chlorides, bromides, iodides, and solubilities of the alkali chlorides increased in the order: potassium, sodium, rubidium, lithium. Veimarn[241] concluded that in most cases the solvent powers of alcohols for inorganic salts decreased with increase in complexity of the

---

* This table is intended merely to summarize a few rather extensive investigations; no attempt has been made to collect all the data available in the literature on the solubilities of inorganic compounds in alcohols.

† The data given by Herz and Kuhn indicate that the values which they reported are for solubilities in *n*-propyl alcohol; no indication is given by Turner and Bissett as to whether *n*-propyl or *iso*-propyl alcohol was used in their work.

‡ Solubility values for lithium chloride, in all cases at variance with these, were obtained by Patten and Mott[238].

§ Centnerszwer[239] determined the solubility of potassium iodide in methyl alcohol at temperatures from 0° to the critical point of the mixture. The curve rose sharply at temperatures above the normal boiling-point of the alcohol, attaining a maximum (29.7 g. of salt per 100 g. solution) at about 190°.

structure of the alcohol, so that for this purpose MeOH > EtOH > PrOH > BuOH > AmOH.

For anhydrous salts it may be stated in general that if the addition of alcohol to water decreases the solubility of the salts, the solubility is least in absolute alcohol; the anhydrous salts of the alkali metals are slightly more soluble in aqueous than in anhydrous alcohols. Gerardin[242] plotted solubility values for several salts in ethyl alcohol of strengths increasing to 94%, and by extrapolation obtained results indicating that the salts studied were insoluble in absolute alcohol. This extrapolation was not valid; the solubilities in absolute alcohol of the salts (NaCl, KCl, Pb $(NO_3)_2$, NH_4Cl, etc.), while slight, were appreciable. Schiff[243] found that the solubility of salts in 40% methyl alcohol was greater than in the same strength of ethyl alcohol. Anhydrous copper sulfate was slightly soluble in absolute methyl alcohol, giving a light blue solution; a trace of water precipitated $CuSO_4.3H_2O$. This solubility of copper sulfate was first noted by Klepl[244], who recommended the appearance of a blue tint as a test for absolute methyl alcohol;* de Forcrand[245] showed that the color of the solution was due to the formation of $CuSO_4.2MeOH$.

Hydrated salts were as a rule less soluble in dilute alcohol than in absolute alcohol; solutions in absolute methyl alcohol of a number of hydrated sulfates gave unstable solutions, the salts crystallizing out after a few minutes (Zn, Cu, Co, Mg) or within a few days; only $NiSO_4.6H_2O$ gave a stable solution. Hydrated salts tended to crystallize with less water of crystallization than was originally present, or with both water and alcohol of crystallization (BaBr$_2$.2H$_2$O separated as the monohydrate; both $NiSO_4$ and $MgSO_4$ took $3H_2O.3MeOH$ instead of 6 or $7H_2O$). Simon[246] found that lithium and magnesium chlorides took both methyl and ethyl alcohol of crystallization. The presence of water in methyl alcohol had a striking effect on the solubility of hydrated salts: the solubilities of $CoSO_4.7H_2O$ in 100%, 90%, and 50% alcohol at 3° were respectively 42.8, 13.3, 1.8, and of $NiSO_4.6H_2O$ at 18°: 31.6, 7.8, 1.9. This effect, while most marked with sulfates, was shown also by other hydrated salts:

---

* The appearance of a similar color (for a different reason, of course) indicates the *presence* of water in ethyl alcohol.

$BaBr_2.2H_2O$ had solubilities (15°) 45.8, 27.3, 4.0 in alcohols of the above-mentioned concentrations. There was apparently a minimum of solubility for such salts in alcohol of about 50% strength.

The use of *iso*amyl alcohol as a reaction medium for inorganic salts was investigated by Curtis and Burns[247]. Pucher and Dehn[248] determined the solubilities of some forty-five organic compounds in absolute ethyl alcohol, quinoline, and mixtures of the two solvents. They found abnormal solubilities for a number of the solutes, and were able to explain these by postulating the formation of addition compounds, some of which they were able to isolate. Herz *et al* studied the solubilities of inorganic salts in mixtures of acetone and water[249], alcohol and water[250], glycerol and water[251], of alkali halides in mixtures of alcohol or glycerol and water[252], of mercuric salts in mixtures of alcohol and water and of ethyl acetate and water[253], and in mixtures of methyl and ethyl alcohols[254], and of inorganic salts in mixtures of methyl, ethyl, and propyl alcohols[237]. Of all mixtures worked with, the mixtures of ethyl and propyl alcohols seemed to have the greatest solvent power for inorganic salts.

Potassium hydroxide dissolved in absolute alcohol is a frequently-used reagent which for quantitative work must be capable of standardization. Difficulty is often encountered in obtaining a solution which will not darken and decrease in strength, and a number of methods of specially purifying the alcohol for this purpose have been proposed. The following method of preparing alcoholic potash from ordinary absolute alcohol was suggested by Malfatti[255]. The potassium hydroxide and a little more than the same weight of calcium oxide were ground to a paste with a little alcohol. The remainder of the alcohol was then added and the mixture was shaken until the potassium hydroxide dissolved; the solution was then filtered and standardized. For more than a year, the author reported, the solution remained colorless and of the original strength. McCallum[256] stated that if ordinary methyl alcohol, without special purification, was used as solvent, alcoholic potash which was entirely stable towards light and age could be prepared; this solution was for analytical purposes in all ways as satisfactory as the usual solution in ethyl alcohol.

Methyl Alcohol as a Solvent.

Methyl alcohol, though possessing various advantages as a solvent, has by no means found as extensive use as has ethyl alcohol. In some cases, however, methyl alcohol has given satisfactory results after the more frequently-used solvent has been tried in vain. In attempts to prepare crystalline bebeerin from a mixture of alkaloids extracted from Indian mallow, Scholtz[257] found that while the extract dissolved readily in ethyl alcohol, it invariably separated in an amorphous condition. Chloroform and acetone gave the same results, but when methyl alcohol was used, the pure alkaloid crystallized without difficulty.

Orndorff and Kennedy[258] fractionally crystallized a mixture of 2,5- and 2,7-dinitrotetrachlorofluoran from acetone and from glacial acetic acid in attempts to obtain the 2,5 compound in a pure state, but neither solvent seemed to effect any separation. Extractions with ethyl alcohol raised the melting point somewhat, but methyl alcohol was found still better for this purpose. The mixture was repeatedly extracted with methyl alcohol; the more soluble portion after several crystallizations gave a sharp melting point and was shown to be the pure 2,5 derivative. Reade and Sim[259] were able to prepare a certain quaternary ammonium perhalide in a state of purity by crystallizing from methyl alcohol; higher-boiling solvents were not satisfactory. Ruhemann[260] and Stäger[261] used methyl alcohol as a solvent to extract the sludge-forming constituents of mineral oils.

Ethyl Alcohol as a Solvent.

Because of its ready availability and wide range of solvent powers, **ethyl alcohol** has been used as a medium for organic reactions far more than any other solvent except water, and in many cases, as the preparation of dry diazo compounds by the method of Knoevenagel[262], has enabled results to be attained which were quite precluded when water was used as a solvent.

The possibility of the solvent being acted upon chemically by the solute or by the reaction for which it is a medium must be taken into account when alcohol is used. Instances have been mentioned above (page 10) wherein alcohol, used as a solvent, was esterified by organic acids in the presence of ammonia as a condensing agent. A similar reaction may take place even if no condensing agent is present. Holland[263] found that while a preliminary crystallization of crude fatty acids from alcohol was desirable to eliminate unsaturated acids, the customary few minutes boiling with alcohol to bring about solution caused a serious drop in the neutralization numbers of the acids, particularly of stearic and myristic. Emerson and Dumas[264] observed that if palmitic acid was dissolved in alcohol and the solution evaporated on the water bath, about 0.3% of the acid was esterified. On the other hand, Bishop *et al*[265] considered that the use of alcohol was advantageous as a solvent in the titration with alkali (or with alcoholic sodium ethylate) of fatty acids, not only because of its solvent power for the materials under examination, which are not soluble in water, but because of increased sharpness of end-point. It was found possible in this way to attain an accuracy of better than 0.5%.

An experience of Lassar-Cohn[266] illustrates the difficulties that may be encountered if an acid crystallized from alcohol is used for determination of formula by ultimate analysis. Dehydrocholic acid, prepared by the oxidation of cholic acid with bromine, was crystallized from alcohol and analyzed. The results obtained did not at all correspond with those calculated for dehydrocholic acid; repeated crystallizations of the acid from alcohol gave results even more in error. It was finally shown that the false results were due to the presence of the ethyl ester of the acid; when the acid was crystallized from acetone the predicted analytical result was obtained. It had been noted that cholic acid crystallized from alcohol in very low yields; investigation showed that this result also was due to esterification. In this case, however, the ester was more soluble than the free acid, so that error was not introduced into the analysis of the acid.

Alcohol may cause other changes in the solute besides esterification. Semper and Lichtenstadt[267] found that if a nitrobenzazoxazin carboxylic acid was dissolved in cold alcohol, the ethyl ester was formed, but that if the acid was added to boiling alcohol, it evolved its carbon dioxide quantitatively, giving nitrobenzazoxazin of sharp melting point, and without a trace of ester. Jackson and Beggs[268] obtained pentabromoacetone melting at

76–7° by crystallizing from ether, chloroform, or benzene, but when alcohol was used, the product melted several degrees lower, and the solution, at first neutral, became acid after a few hours, and smelled of bromoform. Biltz[269] removed methyl alcohol of crystallization from various glyoxalone derivatives by shaking them with ethyl alcohol; in some cases, however, the result was merely the replacing of one solvent of crystallization by the other. A part played by alcohol present in a reaction mixture, quite different from those just mentioned, was reported by Swensson[270], who found that alcohol added to a toluene or xylene solution of bromine exerted a marked negative catalytic effect on the bromination of the hydrocarbon.

Aside from alcohol of crystallization, combined water may occur in crystals which separate from alcohol. Stanbridge[271] stated that carefully dehydrated calcium benzoate formed a very unstable dialcoholate, but that if the trihydrate was crystallized from strong alcohol, the monohydrate was obtained. Hesse[272] reported that hyoscine hydrobromide crystallized from water with 3 H_2O, from 60–80% alcohol with 2 H_2O, from 93% alcohol with 1 H_2O, from 97% alcohol with $\frac{1}{2}$ H_2O; if absolute alcohol or acetone were used the crystals were without solvent of crystallization.

The optimum concentration of the alcohol used as a solvent is at times a factor to be considered. While in the majority of cases it is probably true that, in mixed solvents, as the concentration of one constituent increases from zero to 100% the maximum solubility of a given solute is at one or the other extreme of solvent composition, Holleman and Antusch[273] observed that the alcoholic solution giving the maximum solubility for half a dozen compounds varied from 83% (benzamide) to 95% (α-acetonaphthalide), and Willstätter[274] stated that proper dilution of ethyl alcohol or of acetone (but not of methyl alcohol) materially increased the solvent power of these liquids for chlorophyll. Mylius[275] noted an interesting example of this effect in the case of barium choleate, which was insoluble in absolute alcohol and in water, but which dissolved when a little water was added to a suspension of the salt in absolute alcohol. From apparent physical changes of the salt before solution it seemed probable that a hydrate $C_{25}H_{41}baO_4.3H_2O$ was formed on addition of the water, and that this hydrate was soluble in alcohol.

Dilution of solvent alcohol may have very different effects on different solutes. Both benzene and hexane are completely miscible with absolute alcohol, but according to Sidgwick and Spurrell[276] 90% alcohol will dissolve four times its weight of benzene but only one-third of its weight of hexane. Wood[277] found what seemed to be almost a "critical strength" for aqueous alcohol used as a solvent for volatile oils. Below this point, which was 70% or higher, according to the oil, the solubility was very slight, but when the point was passed, a slight further strengthening caused a marked increase in the solvent power of the alcohol. Somerville[278] reported that a solution of West Australian sandalwood oil in aqueous alcohol possessed abnormal solubility characteristics, in that a concentrated solution of oil, on dilution with more of the same solvent, could be made to precipitate oil. No adequate explanation was given of this phenomenon. Kiliani[279] found that digitonin crystallized readily from 85% alcohol, forming crystals which contained five molecules of water. If the alcohol was either stronger or weaker, the product was in part amorphous, and if the crystallization took place at a temperature lower than 40–45°, the crystals separated in a form which was difficult to filter.

The dilution of alcohol is apt to have an influence, favorable or otherwise, on the course of a reaction for which it serves as solvent or component. Hunt[280] pointed out that in the preparation of ethyl iodide it was better to use 80% alcohol than absolute; the yield was not decreased, and the diminution of the vigor of the reaction allowed much more rapid addition of the required amount of iodine to the mixture of alcohol and red phosphorus. On the other hand, Hall[281] obtained a quantitative yield of triammonium citrate when ammonia was passed into a solution of anhydrous citric acid in absolute alcohol, but when 95% alcohol was used as a solvent, the yield was barely 40% of the theoretical.

Kiliani[282] gave the following details of the method which he used to determine the optimum crystallization mixture for preparing pure digitalin from the technical product. A few decigrams of the latter were dissolved in the minimum quantity of water (about two parts) and absolute alcohol was added dropwise until a slight cloudiness resulted; crystal needles appeared in a few hours, and in two days the crystallization was practically complete. Directly after the addition of the alcohol, the quantity added was ascertained by noting the increase in weight of the container, and it was thus determined that the best solvent for the crystallization was 85% alcohol; another experiment showed that four parts of this solvent were necessary. Using quantities thus fixed, it was possible to recover 43–45% of the digitalin as excellent crystals in a single operation.

In an investigation of the dinitro derivatives of dichlorobenzene, Macleod *et al*[283] carried out the separation of the isomeric 2,6-, 2,5-, and 2,3-compounds by the use of alcohol as a crystallizing medium. On cooling with ice a solution of one hundred grams of the mixture of isomers in three liters of alcohol, the 2,6-derivative separated in a nearly pure state. It was found that if the filtrate was distilled, limiting the quantity of distillate to between 600 and 650 cc. per liter of filtrate in winter, or between 700 and 750 cc. in summer, and the residue allowed to cool very gradually in the water bath overnight, there separated a fraction of definite melting point, consisting of a molecular compound of the 2,6- and the 2,5-derivatives. Pure 2,5-derivative might be obtained from this by treatment with alcoholic ammonia. When the quantity of alcohol distilled varied much from the limits given, a mixture of the molecular compound and the 2,3-derivative was obtained on cooling. The filtrate from the molecular compound gave fairly pure 2,3-derivative when cooled in a freezing mixture.

Occasionally the availability of alcohol as a crystallizing solvent may be increased by the addition of acid or ammonia. Difficulty had been experienced in the preparation of crystalline caffein sulfate until Biedermann[284] used alcohol strongly acidified with sulfuric acid. Hoffmeister[285] suggested the use of alcohol saturated with ammonia as a crystallizing medium for certain amino acids; two or three crystallizations of brown, oily crude leucine or tyrosine gave an almost colorless product. By crystallizing from alcohol containing an excess of ammonia and allowing the product to stand for some time over sticks of potassium hydroxide in an atmosphere of ammonia, Noyes and Goebel[286] were able to prepare ammonium acetate of particular purity.

Lassar-Cohn[287] seems to have been practically the only investigator to use alcohol as a solvent with which to extract aqueous solutions. He found that 90% alcohol readily extracted the potassium salts of some organic acids from an aqueous solution rendered non-miscible with alcohol by saturation with potassium carbonate. This method, here used for the isolation of tauric and cholic acids from a hydrolysis solution, would appear to have wide possibilities of usefulness. Fühner[288] determined the solubilities of the four lowest aliphatic alcohols in aqueous potassium carbonate solutions of various concentrations. Fifty cubic centimeters of solution containing twenty grams of potassium carbonate and saturated with alcohol contained only nine volume percent of ethyl alcohol or one and eight-tenths volume percent of propyl alcohol.

Thompson *et al*[289] purified crude mustard gas by extraction with 92.5% alcohol. The crude material was extracted at a temperature slightly above the critical point of solubility (38.6°). Most of the sulfur, together with a tar-like mass, remained insoluble. The supernatant solution was removed and cooled considerably below the critical temperature, causing the formation of two liquid phases, the upper phase being primarily a solution of dichloroethyl sulfide in alcohol, and the lower phase a solution of alcohol in dichloroethyl sulfide. Crystals of the solid sulfide were obtained by sufficient lowering of the temperature.

CHAPTER IV

THE PREPARATION OF ABSOLUTE ALCOHOLS*

One of the difficulties connected with the use of ethyl alcohol as a solvent is the fact that by simple distillation it can never be completely freed from water. This is due to the fact that ethyl alcohol — and, according to Young and Fortey[294], all higher aliphatic alcohols, but not methyl — forms with water a mixture of minimum boiling point; this mixture, at a pressure of 760 mm. contains 95.57% of ethyl alcohol by weight[294], or 97.17% by volume at 15.56° C.[295]. From such a mixture the water can be removed efficiently only by chemical action, or by the addition of salts with which it can form hydrates.

The constant-boiling mixture, currently known as "95% alcohol," is satisfactory for the majority of solvent uses of alcohol, but in certain cases the presence of even a small amount of water is fatal to the success of the work. Adams and Marvel[296] found that in a condensation in which sodium ethylate was used as a condensing agent, yields of 90% or more were obtained when the alcohol was entirely free from water, but the use of 98.4% alcohol decreased the yield to 66%. Referring to another condensation of this type, Dox and Yoder[297] stated that the presence in the alcohol of a few tenths of a per cent of water greatly reduced the yield of the condensation product. Shepard and Ticknor[298] reported that *o*-hydroxybenzal-*β*-phenyl ethylamine ($Ph.CH_2.CH_2.N : CHC_6H_4OH$) could be reduced in absolute alcohol with sodium, two hydrogen atoms adding at the double bond. If however the alcohol used contained even one or two per cent of water, practically no reduction took place, and phenylethylamine, from hydrolysis of the Schiff's base, was the only base obtained. Fischer[299] observed that in absolute alcohol the solubility of sodium picrate was about five times as great as in 95% alcohol.

---

* The bibliography of the literature on alcohol and alcoholometry compiled by McKelvy, and forming part of one of the bulletins of the Bureau of Standards[290] is an almost inexhaustible source of references, and has been of no small assistance in the preparation of this chapter. The literature on certain phases of the subject was reviewed by Plücker[291], and Patart[292] summarized the development (to the end of 1923) of industrial processes used in France for preparing absolute alcohol. Pique[293] has carefully reviewed the French patent literature on the purification and dehydration of alcohol, and has given a detailed discussion of the processes for dehydrating alcohol which were in use in French distilleries at the close of 1923.

Caspari[300] seemed to find that all absolute alcohol gave an alkaline reaction with various indicators, but Kebler[301] proved that this was not the case, and stated that the alkaline reaction observed by Caspari must have been due to an impurity in the alcohol.

Salts as Drying Agents.

The use as dehydrating agents of **anhydrous salts** capable of retaining water of crystallization is common practice in the drying of liquids and the desiccation of solids, and as long ago as 1796 Lowitz and Richter[302] attained a considerable measure of success in drying alcohol by the use of potassium carbonate, potassium tartrate, and calcium chloride. Potassium carbonate, potassium acetate, and sodium sulfate were shown by Soubeiran[303] to be capable of withdrawing some of the water from 82.5% alcohol, but the most efficient of these salts (potassium carbonate) raised the alcohol content only to 94–5%. Calcium chloride dried the alcohol to about the same extent, but the formation of an alcoholate decreased the yield to such an extent that the use of this drying agent was found to be unprofitable. Göttig[304] stated that propyl alcohol gave a similar addition product of the formula $3PrOH.CaCl_2$.

Mendeleeff[305] found that potassium hydroxide could be used to strengthen a weak alcohol, but by its use no product over 99% could be obtained. Mann[306] dehydrated the constant-boiling mixture of *iso*propyl alcohol and water by adding solid sodium hydroxide in an amount equal to at least 20% of the water present. Practically all of the water separated from the alcohol as a layer of aqueous sodium hydroxide solution. This layer was drawn off as soon as possible, and the dried *iso*propyl alcohol distilled to remove a small amount of dissolved sodium hydroxide. Hammond[307] stated that his method for dehydrating ethyl ether in the vapor phase with sodium hydroxide might also be used for dehydrating low-boiling alcohols or any other organic liquid of boiling point lower than that of water.

By the use of calcium chloride and copper sulfate, Mendeleeff[305] achieved results similar to those found when potassium hydroxide was used; this result with copper sulfate is in agreement with that noted by Young[308], though Perkin[309] obtained with copper sulfate an alcohol of density corresponding to only 99.7%. Patents have been issued[310] for processes for preparing absolute alcohol by the use of copper sulfate. Lebo[311] thought it probable that *iso*propyl alcohol dried over anhydrous copper sulfate had a water content of less than 0.10%, but observed that *iso*propyl alcohol does not appear to retain water as tenaciously as does ethyl alcohol.

Hess[312] claimed that 98.6% of the alcohol present in a commercial product might be recovered entirely free from water by refluxing for half an hour over 37.5% of its weight of anhydrous sodium sulfide. Verola *et al*[313] suggested the use of potassium acetate as a drying agent. Kane[314] prepared pure methyl alcohol from wood spirits by saturating the liquid with calcium chloride and distilling. The alcohol combined with the salt and did not pass over at the temperature of the water bath, while the oils and other impurities readily distilled. Water was then added to the calcium chloride alcoholate, and the dilute alcohol was distilled and dried with lime.

Frankforter and Frary[315] studied the system: aqueous alcohol — anhydrous salt — hydrated salt, using potassium carbonate and potassium fluoride. Such a system containing K_2CO_3 and $K_2CO_3.1\frac{1}{2}H_2O$ was at equilibrium at about 25° when the liquid phase was 99.4% alcohol and the partial pressure of the water vapor 1.2 mm., while when KF and $KF.2H_2O$ were present the other phase was 97.5% alcohol and the aqueous tension was 3.5 mm. Potassium carbonate would seem to be the better drying agent of the two, but the fluoride showed two advantages: (1) its action was much more rapid, and (2) the amount of water required for the formation of its lowest hydrate was exceptionally large (62% as against 32% for lime and 13% for potassium carbonate) so that a much smaller quantity of the salt was required. Frankforter[316] proposed the use of a mixture of potassium fluoride and potassium carbonate for the preliminary drying of alcohol which was to be rendered absolute.

An English patent [317] stated that alcohol to be used for blended fuels could be much more readily dehydrated after being mixed with gasoline. Treatment of a gasoline solution of 95% alcohol with sodium or potassium carbonates gave a product similar to a solution of 99.5% alcohol in gasoline.

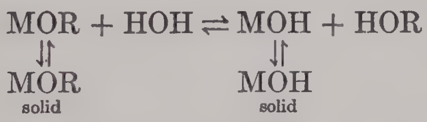
Glycerol as a Drying Agent.

It is well known that pure **glycerol** readily takes up a certain proportion of water which it retains tenaciously at the boiling point of water and even beyond that temperature. Knecht and Muller[318] made use of this fact in the laboratory preparation of 99.5% alcohol. Commercial alcohol was distilled with one-fifth its volume of pure glycerol until the thermometer (bulb in vapor) reached 80°; the distillate was redistilled with about one-sixth its volume of glycerol. The product contained only 0.5 weight percent of water, and was obtained in 84% yield; by heating the glycerol to 180° practically all the dissolved alcohol might be recovered. The expense of the glycerol used in this method was not excessive, and there were the advantages over the ordinary lime method that dehydration was instantaneous, and that there was no loss of alcohol.

Dehydration of alcohol by glycerol had previously been studied (as a possible industrial process) by Mariller[319]. By passing the vapor of 93–95% alcohol up a twenty-plate column down which glycerol was allowed to flow, he was able to obtain 98.5–99% alcohol by the action of commercial glycerol containing 4% water, 99–99.2% alcohol when anhydrous (" dynamite ") glycerol was used, and 99.8–100% alcohol by the action of a 25–30% solution of potassium carbonate in anhydrous glycerol. The glycerol solution of the salt was prepared as indicated on page 79; potassium carbonate was by far the best of several salts used. The volume of glycerol passed down the column in a unit of time was about equal to the volume of strong alcohol which was collected as distillate. An industrial process based on Mariller's work was patented by his collaborator van Ruymbeke[320]; another industrial process for dehydrating alcohol by glycerol was patented by Schneible[321]. Mariller pointed out that for a discontinuous distillation (such as would normally be carried out in the laboratory) the glycerol and the alcohol should be thoroughly mixed (preferably while warm), as otherwise the hydrous alcohol, floating on the glycerol during distillation, would not be effectively subjected to dehydration. The mixture of glycerol, alcohol, water, and dissolved salt remaining after the anhydrous alcohol had passed over was heated to 150° under atmospheric pressure to recover the dissolved alcohol, and was then heated under reduced pressure to drive off the water, as indicated above.

Theory of Dehydration by Chemical Action.

The customary methods of preparing absolute alcohol depend upon chemical action of the water present either with a metal, as calcium or an amalgam, or with a metallic oxide, as lime. While numerous investigators have reported on various practical aspects of the drying problem, only recently has the theory of the process been analysed and used as a foundation for experimental work. Brunel *et al*[322] based their considerations on the fact that when a metal or a metallic oxide is used to dry an alcohol, the following equilibria must be established as soon as hydroxide is formed:



$$\begin{array}{ccccccc} \mathrm{MOR} & + & \mathrm{HOH} & \rightleftharpoons & \mathrm{MOH} & + & \mathrm{HOR} \\ \downarrow\uparrow & & & & \downarrow\uparrow & & \\ \underset{\text{solid}}{\mathrm{MOR}} & & & & \underset{\text{solid}}{\mathrm{MOH}} & & \end{array}$$

M representing the metal and R the alcohol radical. The effectiveness of the drying agent will thus depend primarily on the solubilities of MOH and MOR; the solubility of the hydroxide should obviously be as small as possible, while ready solubility of the alcoholate will have the advantage of allowing equilibrium to be attained more rapidly.

Lime.

According to Smith[323], 50 cc. of 98% alcohol dried over lime contain less than 0.5 mg. of non-volatile matter; from the theoretical considerations just mentioned, **lime** should therefore be very effective for preparing absolute alcohol. In point of fact, its use in investigations requiring high accuracy has shown drying efficiency which could hardly be improved upon. The use of lime possesses the additional advantages that there appears to be no chemical action between the lime and the alcohol, and that the only loss of alcohol is that due to absorption by lumps of lime so large that the alcohol is not readily driven off by heat. The ordinary laboratory procedure for producing absolute alcohol by heating 95% alcohol with lime and then distilling has been applied to large-scale work[324]. Pique[325] has reviewed a considerable number of technical processes used in France for dehydrating alcohol with lime.

It is customary to use a considerably larger quantity of lime than is theoretically required. Kailan[326] recommended a single treatment with about 0.55 kg. of lime per liter of 95% alcohol; this is about three times the calculated amount. Noyes[327], on the other hand, used only 2200 g. lime for eight liters of 92% alcohol; after heating over night the distillate was 99.6–7%. Even by long heating of the residual lime on the steam cone, Noyes was not able to keep the loss of alcohol below 7–8%. For the complete desiccation of an alcohol stronger than 99%, Noyes recommended the use of a quantity of powdered lime not more than 50% in excess of the theoretical amount. After refluxing for 20–40 hours, a distillate of 99.9% concentration was obtained with an alcohol loss of not more than 2%.

Warren[328] conducted the dehydration in two stages, using each time a quantity of lime only slightly in excess of that theoretically required to combine with the water present. He found that although the yield was improved about twenty per cent, the operation took twice the time of a single treatment with a large excess of lime, and no alcohol could be obtained stronger than 99%. The method found most satisfactory by Smith[323] was to add to ordinary alcohol the quantity of lime calculated to bring the alcohol to 98%; the mixture was allowed to stand for about a week and was then filtered. By refluxing this 98% alcohol for about two hours over 120 g. lime per liter of alcohol, an entirely anhydrous product could be distilled off with a minimum of loss.

Opinions differ as to the optimum time and temperature for the drying reaction. Kailan[326] found that at 20°, 175 hours contact of an alcohol originally 95% with rather more than half its weight of lime gave a product containing 99.4% alcohol, and that after 575 hours the strength was 99.95%. Soubeiran[303] obtained a 99.5% product after 24 hours contact at 35–40°. Erlenmeyer[329] claimed that after refluxing over lime for an hour all the distillate was 100% alcohol, but Kailan[326] reported that after 3.5 hours boiling the alcohol was only 99.5%, and after six hours 99.9%. Wightman *et al*[330] prepared 99.96% alcohol by drying with lime in two stages, digesting for several days each time. Mendeleeff[305] and Andrews[331], using alcohol 99% or stronger, agreed that two days at room temperature or about an hour under a reflux condenser gave the maximum amount of drying.

Noyes[327] observed that the distillate of very nearly absolute alcohol was always turbid. He thought at first that lime was carried over mechanically, but a very efficient trap failed to prevent the turbidity. In one case, distillates (from lime) of strengths 99.92, 99.98, and 99.99% contained, as shown by titration with standard acid, 5.0, 12.0, and 22.5 mg. of calcium per liter respectively. It seemed probable that the calcium volatilized as calcium ethylate and that this was converted to the hydroxide by a trace of moisture. Redistillation of the turbid alcohol gave a clear distillate, if exposure to the air was avoided.

Squibb[332] tried to accomplish the last stage in the dehydration of a 99.8% alcohol by shaking it vigorously with lime, in order to attain more complete contact of the two phases. In a short time an almost unfilterable mixture was formed, so this method was abandoned in favor of repeated percolation of the alcohol through a column of carefully ignited lime[333], followed by distillation, in some cases under reduced pressure. This last precaution was for the purpose of removing dissolved air when the alcohol was to be used for density determinations. Danner and Hildebrand[334], in considering the effect of temperature on the rate of drying, postulated the formation of a thin film of insoluble calcium hydroxide over the surface of the lime, which then almost completely stopped further reaction. To prevent the formation of this film, they shook very vigorously the mixture of alcohol and lime, and in the last stage of the desiccation used calcium oxide in the form of an extremely fine powder. Harned and Fleysher[335] found that in drying alcohol with lime, vigorous shaking at regular intervals was essential. Osborne and McKelvy[336] noted that freshly-ignited lime was not necessary to obtain an alcohol of very low density. Crismer[337] and Gyr[338] observed that methyl alcohol could not be satisfactorily dried with lime.

Soubeiran[303] and Mendeleeff[305] seemed to find that alcohol refluxed too long over lime, or distilled at too high a temperature, extracted water from the calcium hydroxide, and Andrews[331] noted the same effect when metallic calcium or magnesium amalgam was used. Brunel *et al*[322] questioned such a dehydration of lime from the theoretical consideration that even at 117° (the boiling point of butyl alcohol) the vapor pressure of water over a mixture of calcium oxide and calcium hydroxide would be approximately 0.00002 mm.* They added freshly slaked lime, dried at 200°, to thoroughly dried butyl alcohol, and observed that the boiling point was not altered by so much as 0.002°. Since, according to Johnston† the aqueous tension of magnesium hydroxide is about 1 mm. at 25°, Andrews'[331] result with magnesium amalgam is more probable. An alcohol in which the partial pressure of water was 1 mm. at 25° would contain about 0.5% water.‡ The fact shown by Crismer[337] that absolute methyl alcohol becomes moist on contact with calcium hydroxide, even at ordinary temperatures, would seem to invalidate the contention of Brunel *et al*[322] that the pressure of aqueous vapor over a dehydrating agent was a measure of the ability of the agent to dry alcohol. Indeed, the latter investigators stated that aluminum hydroxide, which dissociates partially at 200°, might well give a sufficient dissociation pressure of water at the boiling point of the higher alcohols to prevent their thorough drying with aluminum amalgam, yet they did not find this to be the case, and Konek[341], as described later, prepared absolute alcohol by refluxing aqueous alcohol over magnesium amalgam and distilling, though the figures of Johnston* show that at the boiling point of alcohol the aqueous tension of magnesium hydroxide, which is formed in the reaction of dehydration, is greater than the partial pressure of water in boiling 95% alcohol.

---

* This value was obtained by extrapolation of the data given by Johnston[339].

† The values given in the paper by Johnston previously cited[339] for the pressure of water vapor in equilibrium with magnesium hydroxide at various temperatures do not altogether agree with those found by the same author and published elsewhere[340]. In a private communication, Dr. Johnston has informed the writer that various sources of error so influenced the accuracy of these determinations that it is safest to use the rounded value of 1 mm. and 100 mm. for the aqueous tension of magnesium hydroxide at 25° and 78° respectively.

‡ Interpolated from the data of Frankforter and Frary[315] quoted above.

Barium Oxide.

The use of **barium oxide,** either alone or in conjunction with lime, was proposed by Berthelot and St. Gilles[342]. The alcohol was first treated with lime, and was then digested with barium oxide until the solution took on a yellow tinge; the alcohol was then decanted and distilled. Mendeleeff[305] obtained better results by distilling directly from the oxide rather than decanting, and observed that the appearance of the yellow color furnished a very convenient means of telling when the alcohol was entirely dehydrated. He cautioned, however, against letting the mixture stand too long; after a week the solution was orange-red, and the distillate was of much too high gravity. More recently Noyes and Warfel[343] found it convenient to add a little barium oxide to the lime used for the last stage of a desiccation; the middle cut of their distillate contained 99.98% alcohol.

Brunel *et al*[322] found that barium oxide was somewhat more rapid in its action than was lime. It did not seem to dry the alcohols more thoroughly than lime, but they stated that this was not surprising, since any further reduction in the amount of water below what could eventually be reached with lime, probably could not be detected. Experiments by Crismer[332] indicated that while barium oxide unquestionably dehydrated wet alcohol, the tendency to form an ethylate brought about a state of equilibrium before complete absence of water was attained.

Cook and Haines[344] observed that barium oxide was not suitable for drying methyl alcohol, since, like calcium chloride, the drying agent combined with the alcohol. Vincent and

* See second footnote, page 58.

Delachenal[345] noted the formation of a compound $2C_3H_6O.BaO$, which rendered inadvisable the use of barium oxide for drying allyl alcohol.

Calcium.

Winkler[346] suggested the use of **metallic calcium** in the dehydration of alcohol. A commercial absolute alcohol was refluxed for a few hours with about twenty grams of calcium shavings per liter. After a few hours the evolution of hydrogen ceased, and the distillate was alcohol of 99.9% purity. Careful determinations carried out by Goldschmidt and Sunde[347] indicated that alcohol dehydrated with calcium was superior in strength to absolute alcohol from lime. Lapworth and Partington[348] removed the last traces of moisture from samples of alcohol dried over lime by heating the alcohol with a considerable excess of calcium turnings until a sample of the liquid on addition of water set to a jelly-like mass, indicating that calcium ethylate was present. Loriette[349] patented a process whereby alcohol was freed from water by bringing the vapors in contact with lime and then with metallic calcium or calcium carbide.

Perkin and Pratt[350] doubted the practical availability of the calcium method because of the rapid formation of alcoholates; for higher alcohols this reaction was slow at room temperature, but at the boiling point of the alcohol was complete within a few hours. Andrews[331] observed that alcohol from calcium sometimes possessed a peculiar foreign odor, and Osborne *et al*[351] found that alcohol prepared in this way had a slightly high density, but Crismer[337] stated that the critical temperatures of solution were the same for samples of alcohol dried with calcium and with lime.

As Moissan[352] pointed out, calcium nitride reacts slowly with alcohol, forming calcium ethylate and ammonia. Winkler[353] reported that calcium prepared by filing clean pieces of metal was practically free from calcium nitride; by discarding the first part of the distillate an alcohol wholly free from ammonia was obtained. Commercial calcium filings contained a considerable amount of calcium nitride; to prepare this material for use the filings were first sifted on a fairly coarse screen to remove the greater portion of the nitride, and were then washed with carbon tetrachloride to remove grease; in this washing a further portion of the nitride was removed. About twenty grams per liter of the cleaned filings were used for drying the alcohol. To the distillate, which was free from water, but which contained ammonia, a few centigrams of alizarin were added. About half a gram of tartaric acid was dissolved in a little of the alcohol; this solution was added to the colored alcohol until the color changed from reddish-blue to pure yellow. A few drops of the acid solution were added in excess, and the alcohol was redistilled, avoiding atmospheric moisture.

Goldschmidt and Thuesen[354] removed ammonia from methyl alcohol which had been dried with calcium by distilling the alcohol twice over anhydrous sulfanilic acid. Picric acid was not satisfactory for this purpose, since traces of it volatilized with the alcohol. Goldschmidt[355] found that the sulfanilic acid method was not satisfactory for ethyl alcohol. For the last step in the dehydration he used freshly scraped calcium wire. An amount of wire equivalent to ten times the water present was used; for an alcohol which was nearly dry this amounted to only a fraction of a gram of calcium per liter. During the refluxing a stream of carefully dried air was passed through the vapor space in the flask to sweep out any ammonia which might be formed. Patents[356] covering the use of calcium for the industrial preparation of absolute alcohol stated that ammonia might be removed by passing the alcohol vapor through burnt alum.

Robertson and Acree[357] obtained an alcohol of minimum specific gravity by using lime and calcium simultaneously. The higher density (in one case corresponding to 0.18% water) obtained when calcium alone was used was explained on the assumption that the alcohol was catalytically decomposed into water and ethylene or ether; Brunel *et al*[322] considered that the trouble might have been caused by ammonia. Calcium was successfully used by Klason and Norlin[358] to dry methyl alcohol. As long as there was water present, a dirty-gray, slimy precipitate remained after distillation of the alcohol; when all the water had been removed, the calcium dissolved completely, and left a pure white crust of calcium methylate. Gyr[338] noted the same effect, and, in common with Winkler[346], remarked on the increased vigor of the reaction as the water content of the alcohol became less. All investigators agree that when calcium is used repeated treatments are necessary to obtain complete dehydration.

Bjerrum and Zechmeister[359] found that absolute methyl alcohol could be prepared by a single treatment with **magnesium** ribbon (ten grams for each liter of alcohol). They stated that magnesium ribbon was cheaper than metallic calcium and more convenient to handle than magnesium amalgam.

Sodium.

When the ready solubility of sodium hydroxide in alcohol is considered in the light of the equilibrium equation stated on p. 55, it can readily be seen that the use of **sodium** or its amalgam for the preparation of absolute alcohol (first suggested by Mendeleeff[305]) would be of doubtful efficiency. Squibb[333] reported that an unsatisfactory product was obtained by the use of sodium ribbon, even when the moist alcohol was maintained at a temperature of $-17°$ to decelerate the formation of ethylate; similar negative results have been obtained by Crismer[337] and others. By distillation of partially dried alcohol over sodium, Kailan[360] was not able to get an alcohol stronger than 99.7% whereas alcohol heated for fifteen hours with two-thirds its weight of lime gave a product of 99.90–99.97% alcohol content.

On the other hand, Goldschmidt[361] found only 0.20% of water in alcohol dried over sodium, and Keyes and Winninghoff[362] were able in this way to prepare propyl and *iso*amyl alcohols of specific conductances no greater than 2.0×10^{-8}. Similar results for *iso*amyl alcohol were obtained by Kraus and Bishop[363], who attained a still greater degree of purity by subjecting their product to fractional condensation under reduced pressure. Marvel and Tanenbaum[364] found that if in the preparation of phenoxybutyl alcohol, ethyl alcohol dried over lime was used as solvent, yields of not over 45% were obtained, while if this alcohol was further dried over sodium, yields of 62–68% were insured.

Crismer[337] obtained good results on drying methyl alcohol by repeated treatments with small quantities of phosphorus trichloride, but considered sodium the best material for this purpose. He showed conclusively that methyl alcohol was capable of extracting water from calcium hydroxide. McKelvy and Simpson[365] prepared very pure methyl alcohol by carrying out the preliminary drying by distillation from lime, but the last traces of water were removed by treatment with sodium, since when lime was used for the final dehydration, great swelling of the lime occurred, and loss of alcohol resulted. Two distillations from sodium were necessary before a constant composition was obtained. Claisen[366] observed that since alcohol readily absorbs acid vapors, alcohol which must be entirely neutral should be distilled over sodium just before use.

Friedel and Crafts[367] found that methyl alcohol sufficiently dry for the preparation of silicon tetramethylate could be obtained only by distilling very pure alcohol several times over sodium, and finally distilling once over a little phosphorus pentoxide. They prepared a still drier alcohol by boiling this material with silicon tetramethylate ($Si(OMe)_4$).

Aluminum Amalgam.

Aluminum amalgam was recommended by Wislicenus and Kaufmann[368] as an excellent reagent for preparing absolute alcohol, since, unlike sodium amalgam, it had no action on alcohol, and might therefore be used freely without fear of loss of alcohol. To prepare the amalgam[369], aluminum wire was etched with 10% caustic until the surface was quite clean, then was washed, and was dipped for a few seconds in a 1% mercuric chloride solution. The wire was washed with water to remove the black slime which formed on the first amalgamation, and was then treated for a longer time with the amalgamating solution. The wire was finally washed rapidly with alcohol, then with ether, and was preserved under petroleum ether. Pozzi-Escot[370] distilled ordinary alcohol over potassium carbonate, obtaining a product of 98–99% strength, and removed the remainder of the water by digesting the alcohol with aluminum filings in the presence of mercuric chloride. Osborne and McKelvy[336] obtained excellent results by the use of aluminum amalgam, and Brunel *et al*[322] found it their most satisfactory reagent, on account of the rapidity and completeness of its action. Clough and Johns[371] prepared anhydrous *iso*butyl alcohol by dehydrating the azeotropic mixture of the alcohol and water (containing about 27% of water by weight) with sodium hydroxide and then distilling over aluminum amalgam.

That unnecessarily prolonged treatment of alcohol with aluminum amalgam is to be guarded against is indicated by the fact that Adkins[372] prepared aluminum derivatives of the four lowest alcohols by refluxing the absolute alcohols with aluminum amalgam; in the case of butyl alcohol the reaction was violent even in the cold. Yields of alcoholate as high as 95% of theory were obtained.

Magnesium Amalgam.

Evans and Fetsch[373] rubbed magnesium powder with eighteen times its weight of mercury, and observed that the amalgam thus formed was without action on absolute alcohol, but readily reacted with alcohol containing traces of water. Konek[341] prepared absolute alcohol by refluxing partially dehydrated alcohol, or even 95% alcohol, for a few hours with an excess of magnesium amalgam and then distilling. Andrews[331] obtained good results with an amalgam prepared by agitating magnesium powder with its own weight of mercury under the surface of 98% alcohol acidified with a little hydrochloric acid. The alcoholic acid was then poured off and the magma washed with absolute alcohol. By the use of this method a large weight of magnesium was rendered available in proportion to the amount of mercury used.

Calcium Hydride.

Calcium hydride was used by Riiber[374] to carry out the last step in the dehydration of alcohol. The alcohol used had been dried with lime to 99.90% strength. Three and one-half grams of calcium hydride, prepared as described by Lindemann[375], were dissolved in about 200 cc. of the alcohol to be purified, and about two-thirds of the alcohol was distilled off. In this way any ammonia present was removed, and the hydride was converted to calcium ethyl. This solution was then added to the main part of the alcohol which was to be purified (about two liters) and the entire solution was gently boiled for about twenty hours under a reflux condenser. During this time a stream of carefully dried hydrogen was passed through the entire apparatus to remove any aldehydes present. Three treatments with calcium hydride gave an alcohol of minimum density. Riiber stated that he was able to obtain equally good drying with lime or with metallic calcium, but that he found the calcium hydride method more rapid, more certain, and more convenient than either of the others.

Calcium Carbide.

The use of **calcium carbide** to remove water from alcohol was recommended by Yvon[376], and was further investigated by Cook and Haines[344]. To prepare absolute methyl alcohol, the latter workers treated the alcohol with a 20% excess of carbide over the amount required to combine with the water present; the use of a reflux condenser was necessary, as the heat of the reaction raised the temperature to boiling. The reaction took four or five hours, during which time the mixture was occasionally shaken. When the evolution of acetylene had ceased, the mixture was refluxed for several hours to drive off the greater part of the dissolved acetylene. The alcohol was distilled and shaken with anhydrous copper sulfate to remove the acetylene still present, and was then redistilled over copper sulfate. The dehydration of ethyl alcohol was carried out in the same way, except that a reflux condenser was not needed. For the treatment of butyl and amyl alcohols it was sometimes necessary to warm the mixture to facilitate reaction. It is needless to say that great precautions were observed throughout the process to avoid danger of explosion.

Frankforter[377] subjected alcohol to a preliminary drying over a mixture of potassium fluoride and potassium carbonate; the alcohol was then heated over lime for an hour at a pressure of 55 lbs. per sq. in. (corresponding to a temperature of about 125° C.). The alcohol vapors, still under pressure, were passed through a tube filled with granulated calcium carbide to remove the last traces of water.

Physical Methods of Dehydration.

The distillation methods of LeBel and of Young and the atmolysis method of Urbain cannot compare in general utility with chemical methods for obtaining alcohol of strength greater than the constant-boiling mixture, though Young[378] stated that the method which he devised had been employed since 1908 by Kahlbaum of Berlin for the production of absolute alcohol from strong spirit, and Pique[379] named half a dozen French distilleries which were using processes of this nature at the close of 1923. These methods may however be cited as the only ways proposed for accomplishing this end by purely physical means.

LeBel[380] observed that on fractional distillation of an alcohol stronger than the constant-boiling alcohol-water mixture, the fractions increased in strength as the distillation proceeded, due to the removal in the first cuts of a part of the water as the mixture of minimum boiling point. He was not able in this way, however, to obtain an entirely anhydrous alcohol. Wade and Merriman[381] showed that the constant-boiling mixture of alcohol and water grew richer in alcohol as the pressure was decreased; by repeated distillations under a pressure of 58 mm. they were able to prepare alcohol of 99.05% strength. Merriman[382] later found that under a pressure of 70 mm., completely anhydrous alcohol might be distilled from a mixture of alcohol and water. This principle has been made the basis of the Barbet method for the industrial preparation of absolute alcohol, as described by Pique[383].

Young[384] found that when a mixture of equal parts of 93% alcohol and benzene was distilled, separation took place into (1) a ternary mixture of alcohol, benzene, and water, boiling at 64.85°, (2) an alcohol-benzene mixture, boiling at 68.25°, and (3) pure alcohol, boiling at 78.3°. With a very efficient still-head, two or three distillations, each time with addition of more benzene, were sufficient to remove all the water, but there appeared to be a trace of benzene left in the alcohol. This was removed by distilling the dehydrated alcohol with *n*-hexane; the binary hexane-alcohol mixture which came over first carried the benzene with it, and no hexane was left in the residual alcohol. The specific gravity of the alcohol obtained in this way indicated practically complete dehydration. Industrial processes based on the use of benzene have been patented by Steffens[385], by Marks[386], by Backhaus[387], and others[388]. Marks[389] and Rodebush[390] patented processes using ethyl acetate as the third liquid. A patent[391] has been granted on a process for drying other organic liquids (*e.g.*, glycerol, propyl alcohol) by Young's method.

One of the chief disadvantages of Young's method is the small temperature difference between the boiling points of the ternary mixture, the binary mixture, and pure alcohol; because of this it is difficult to remove the last traces of benzene from the purified alcohol, and the use of a stillhead of the highest efficiency is essential. Chavanne[392] suggested the use of dichloroethylene instead of benzene: the range of boiling points is greater, and there is less loss of alcohol in the ternary and binary mixtures. Chavanne considered, however, that no modification of this method could compete in general utility with methods of dehydration by chemical means. Guinot[393] preferred trichloroethylene to many other liquids tried as third component, since when this compound was used, the azeotropic mixture, on condensation, separated into a layer of dilute alcohol and a layer containing 99% of the trichloroethylene with practically no water. A continuous dehydration process was developed which made use of this characteristic.

E. and R. Urbain[394] made use of the principle of **atmolysis** (differential diffusion of the components of a gaseous mixture through a porous tube) to obtain nearly anhydrous alcohol. The apparatus consisted of a distilling flask surmounted by a tube of unglazed porcelain; the top of the porous tube was connected with a reflux condenser. The tube was surrounded by a jacket in which reduced pressure was maintained to cause gaseous diffusion. When 95% alcohol was distilled, water vapor diffused in preference to alcohol vapor, and the alcohol remaining in the flask at the close of the treatment was of 99.8% strength.

Estimation of Water.

The most common method of determining the amount of water present in alcohol is by a determination of the specific gravity, and comparison of the value found with carefully prepared tables of the specific gravities of known mixtures. For samples of alcohol more dilute than 90% no better method than this has been proposed, but when it is necessary to determine accurately the small amount of water present in a partially dehydrated alcohol, the determination of density is handicapped by the necessity for large samples, accurate weighing, and thermostatic control, since the presence of 0.1% of water in alcohol changes its specific gravity by only about 0.0003.

A method proposed by Goldschmidt[361] and further described by Gyr[395] was the determination of the **constant of esterification** of the alcohol with some organic acid. To determine this value, 10 cc. of a 0.2-normal solution of hydrochloric acid in the alcohol (this solution must be freshly prepared) and 10 cc. of a 0.2-normal solution of the organic acid were brought to 25° in a thermostat, mixed in a well-stoppered flask, and allowed to stand in the thermostat for the desired length of time — six minutes was suggested — and then titrated. The esterification constant $k = \frac{1}{t} \ln \frac{a}{a - x}$, in which a is the number of cubic centimeters of organic acid present at the beginning of the reaction (20 cc. of 0.1 normal), and $a - x$ the number of cubic centimeters present after the time t (in hours). Acetic acid was not recommended for this work, owing to the speed of the reaction; since 50% of the acid was esterified in about two minutes, a slight inaccuracy in noting the time would have a marked effect on the constant obtained. Better results were secured by the use of phenylacetic acid, which required about five minutes for 50% esterification. Using this acid, k was determined as 3.566 with pure methyl alcohol for a reaction time of 0.1 hour, and 3.235 when t was 0.45 hour.* Goldschmidt found that butyric and propionic acids could also be used with good results.

The purest methyl alcohol prepared by Gyr had a density (15°/15°) of 0.79647 and a k value of 3.566; an alcohol containing 0.125% of water showed a density of 0.79691 and a k value of

---

* This diminution in the esterification constant was explained by Goldschmidt[396] as being due to dilution of the reaction mixture by the water formed in the process of esterification.

3.098. Thus the addition of a trace of water decreased the density by only about 0.055%, but the k value was decreased 13.4%. In specially prepared alcohols containing 0.40% and 0.200% of water, Goldschmidt[361] found by this method 0.43% and 0.198% respectively. Kailan[397] considered that the results obtained by Goldschmidt's method, even under the most favorable conditions, were not as accurate as the values calculated from specific gravity determinations.

Bredig and Fraenkel[398] suggested the velocity coefficient (determined gasometrically) of the decomposition of diazoacetic acid[399] as a means of determining small amounts of water in alcohol. The addition of 0.18% of water to a sample of anhydrous alcohol decreased the coefficient for this reaction from 0.0515 to 0.0396.

In the careful work carried out by Andrews[331] on the action of various drying agents on ethyl alcohol, the progress of the dehydration was gauged by the method suggested by Crismer[400] of observing the **critical solution temperature** of the alcohol in kerosene. The theory of this effect was discussed at length by McKelvy and Simpson[401], and Orton and Jones[402] pointed out that in both binary and ternary mixtures the sensitiveness of the critical points to impurity in one constituent of the mixture was determined by the relative solubility of the impurity and the one constituent in the other constituent of the mixture, so that the remarkable delicacy of Crismer's method is to be attributed to the great difference of solubility of the water and the alcohol in kerosene. To give a sharper reading, Crismer removed some of the volatile constituents of the kerosene by passing steam through it for some time, after which it was dried. Equal parts by volume of alcohol and kerosene were cooled until the mixture became turbid; at that point the temperature was taken. For absolute alcohol, with the kerosene used, this temperature was about 4°; for 99.8% alcohol the temperature was 8°. The sensitiveness of this method for the detection of traces of water in alcohol which was nearly absolute, was indicated by the fact that an increase of 0.1° in the critical solution temperature — a difference readily observed — corresponded to the addition of only 0.005% of water.

Crismer noted the additional advantages that the method was rapid, that it required only a few cubic centimeters of the alcohol, and that neither weighing nor thermostatic control were necessary. He found that the volumes of alcohol and oil used for the test might be varied as much as 10% without appreciably changing the critical solution temperature. For following by this method the progress of the dehydration of amyl alcohol, Crismer[403] recommended glycerol as a more satisfactory solvent than any of the petroleum distillate fractions. Osborne and McKelvy[336] found determinations by the kerosene method both accurate and serviceable in testing fractions of strong alcoholic distillates. On the other hand, Osborne *et al*[351] considered that the sensitiveness of this method did not exceed that of specific gravity determinations, and Robertson and Acree[357] pointed out the disadvantage that the critical solution temperature varied widely with different samples of kerosene.

In an attempt to improve the method by substituting for kerosene some single liquid which could readily be obtained in a very pure state, McKelvy and Simpson[401] determined the critical solution temperature of methyl and ethyl alcohols in carbon disulfide. For the former alcohol a temperature of 35.7° and a critical concentration of carbon disulfide of about 85% by weight were found. The critical values for the system: ethyl alcohol — carbon disulfide were $-24.4°$ and 83% of disulfide. Since the addition of 1% of water raised the critical solution temperature only about 10°, the method using carbon disulfide was not as delicate as the original way with kerosene, but the modified method has the advantage (hardly, it would seem, of prime importance) that the temperatures were not dependent upon the particular lot of solvent used. Kolthoff[404] described a colorimetric method for determining the water content of strong alcohols.

Removal of Aldehyde.

The removal of aldehyde, a common impurity of alcohol, by resinification with potassium hydroxide or by oxidation with permanganate as proposed by Waller[405], is not satisfactory because of the incompleteness of the reaction.

Several methods have been described for oxidizing the aldehyde by silver nitrate or by silver oxide. Wildermann[406] added silver nitrate and a few drops of nitric acid to the alcohol to be purified, and heated the solution for several hours under a reflux condenser. Winkler[346] proposed the use of alkaline silver oxide to oxidize the aldehyde to acetic acid, which was retained by the alkali when the alcohol was distilled. In the original procedure, found successful by Andrews[331] and by Danner and Hildebrand[334], dry silver oxide was used, but Dunlap[407] improved the method by precipitating the oxide in the alcohol to be treated. For each liter of alcohol, 1.5 g. of silver nitrate (or more if the alcohol was very impure) were dissolved in a little water and added to the alcohol, which was contained in a cylinder rather than in a flask; the mixture was well shaken. Three grams of potassium hydroxide (or twice the weight of the silver nitrate used) were dissolved in about 15 cc. warm alcohol, and after cooling, this solution was poured into the alcoholic silver nitrate without stirring. The mixture was allowed to stand until the oxide had all settled, then was filtered and distilled; it was not necessary to reject any of the distillate. This method possessed several advantages over Winkler's method. There was a material saving of time in precipitating the oxide in the solution rather than preparing it beforehand and then utilizing it; more important, the oxide was thrown down in a very minute state of subdivision, and hence in the best state for a rapid and complete oxidation of the aldehyde. If the cylinder was shaken after the addition of the alkali, the oxide gathered in flocks which settled rapidly, and which were thus much less effective than the finely-divided and slowly-settling precipitate. Neither method using silver nitrate was applicable to methyl alcohol.

Rowe and Phelps[408] compared several methods for removing aldehyde, and selected as the best a method attributed to Girard and Cuniasse[409]. This involved the addition of three or four grams of *m*-phenylenediamine hydrochloride to every liter of 95% alcohol. The mixture was allowed to stand for several days and was then fractionated slowly, the middle 50% being taken as aldehyde-free alcohol. It was found that this treatment seemed not only to eliminate aldehydes, but also to remove all except small traces of peroxide. A similar method has been proposed by Windisch[410].

Heuser[411] described a method of removing aldehydes and fusel oil which involved diluting the 95% alcohol with de-oxygenated water to 60–62° proof, agitating the diluted alcohol with chloroform, and after drawing off the chloroform layer, subjecting the aldehyde-free alcohol to vacuum to remove dissolved chloroform. The entire process was carried out in the absence of air.

Osborne and McKelvy[336] hesitated to use any chemical means for removing aldehyde, because of the possibility of contaminating the product, but were successful in the use of the method proposed by Paul[412]. The alcohol was boiled for two days under a reflux condenser through which was passed water at a temperature of 50–60°. The top of the condenser was provided with an arrangement by means of which the more volatile constituents could be drawn off by a current of dry air. At the end of two days' treatment, the most delicate tests failed to reveal any aldehyde, either in the vapor or the liquid, but after the aldehyde-free alcohol had been kept in the dark for a week, tests showed about as much aldehyde as was present before the treatment. Riiber[374] removed aldehyde in a similar manner, except that he used carefully dried hydrogen instead of air, to avoid possible oxidation of the alcohol vapors.

Castille and Henri[413] removed aldehydes and other impurities by adding one gram of iodine to each liter of absolute alcohol, letting the solution stand for twenty-four hours, and distilling slowly, collecting the middle portion of the distillate. The trace of iodine carried over with the vapors was removed by distilling a second time over a little pure zinc powder. The purified alcohol was dried over lime, and was found to be optically pure.

Lanzenberg and Duclaux[414] proposed a special method for removing acetone from methyl alcohol; this impurity is sometimes present in large quantities, and is difficult to separate by simple distillation. The process recommended was based on the fact that methyl alcohol and chloroform form a mixture boiling at 53°, while the acetone-chloroform mixture boils at 65°. One part of alcohol and 7.5 parts of chloroform were distilled, and the fraction boiling at 53° was taken. This fraction was washed three times with water, which extracted all the alcohol, and rectification of this solution gave a product containing only about 0.25% acetone. The recovery was about 72.5% of the original alcohol.

Menzies[415] prepared pure methyl alcohol from crude wood spirit containing 12% of acetone and 6.7% of esters by decomposing the acetone with sodium hypochlorite. Theoretically, three moles of hypochlorite are capable of oxidizing one mole of acetone to chloroform; in practice it was found that if a little less than the theoretical quantity of aqueous hypochlorite was added to the crude spirit, it reacted quantitatively with the acetone. The chloroform layer was drawn off, and an amount of hypochlorite about 50% more than enough to remove the remaining acetone was added. The aqueous alcohol was then fractionated, dried, and redistilled. About 75% of the original alcohol was obtained as acetone-free product, with only small amounts of other impurities.

For the preparation of perfectly neutral alcohol, Carlton[416] first added 10 cc. of concentrated sulfuric acid to each liter of alcohol and distilled. In this way any amines present, together with most of the water, were removed; the alcohol was then distilled from a little potassium hydroxide to remove acidic substances.

Affinity of Absolute Alcohol for Moisture.

Conflicting statements have been made regarding the hygroscopic character of absolute alcohol. Winkler[346] found that alcohol exposed in a beaker to the atmosphere of the laboratory for fifteen minutes took on less than 0.1% of water, and Mendeleeff[305] and Plücker[291] obtained similar results, but Andrews[331] was unable to confirm Winkler's results, and Brunel *et al*[322] stated that even with considerable precautions they were unable to keep their alcohol dry. Crismer[337] reported that a small volume of alcohol exposed in a graduate took on 0.2% of water in 25 minutes, and 0.7% in an hour and a half. Loriette[417] reported that alcohol of any strength above 92% took up about 0.2% of water per day when a layer 5 cm. deep was exposed to moist air. Alcohol of 99.8% strength seemed to absorb moisture no more rapidly than more dilute alcohol.

CHAPTER V

HIGHER ALCOHOLS AND ETHERS AS SOLVENTS

A. Higher Alcohols

In sharp contrast to the wide-spread and diversified use of methyl and ethyl alcohols as solvents, the higher alcohols have only occasionally been used for this purpose, and for the most part their solvent properties are but little known. A probable reason for this may be found in the statement contained in a private communication to the writer that an experimenter needing *iso*propyl alcohol in 1919 found only a single dealer offering it, and at the price of $8.50 per pound. The commercial production of this alcohol has since been developed, and Curme and Reid[418] state that in its general physical and solvent properties *iso*propyl alcohol stands much closer to ethyl alcohol than does any other of the aliphatic alcohols. This generalization was supplemented in a letter from Dr. Curme, above referred to, by the statement that practically all liquids or solids miscible with or soluble in ethyl alcohol are also miscible with or soluble in *iso*propyl alcohol, and that in most cases a rather highly refined measurement is necessary to determine the difference of solubility or miscibility. Winkler[419] suggested the use of propyl alcohol as a solvent for the analytical saponification of fats. Its solvent properties seemed fully as good as those of ethyl alcohol, and its higher boiling point caused reaction to take place more rapidly, and obviated the necessity of a reflux condenser. Grant and Johns[420], Fuller[421], and Valli-Douau[462] discussed the properties of *iso*propyl alcohol as a technical solvent.

Among the occasional instances of the use of **butyl alcohol** as a solvent may be cited the crystallization of *p*-hydroxyphenyl-azo-hydrocupreine carried out by Heidelberger and Jacobs[422]. The crude dyestuff was dissolved in hot commercial butyl alcohol, an equal volume of dry ether was added, and ligroin was added to incipient turbidity. The solution was filtered, seeded, and allowed to stand in the ice-box. The microscopic needles which separated contained one-half mole of solvent of crystallization.

Until recently, the usual method of isolating free hydroxylamine was by fractional vacuum distillation of a solution of hydroxylamine in methyl alcohol. Lecher and Hofmann[423] showed that hydroxylamine could be crystallized from absolute ethyl alcohol with a yield of 40%. Hurd and Brownstein[424], working on the hypothesis that the longer the hydrocarbon chain of an alcohol, the lower would be the solubility of hydroxylamine, tried butyl alcohol as solvent. The yield obtained was 50% of theory instead of 40%, and the procedure was made much simpler, since no special precautions were needed to obtain an anhydrous solvent, and the crystallization was virtually complete at −10° instead of the lower temperature required for complete crystallization from ethyl alcohol.

Pépin-Lehalleur[425] discussed the laboratory use of butyl alcohol and its esters, and pointed out the advantages of lack of hygroscopicity, and ease of recovery from aqueous solutions: butyl alcohol is practically insoluble in water saturated with calcium chloride or with alkali carbonates. According to Pardee *et al*[426] butyl alcohol is superior to ethyl alcohol as a medium for quantitative saponifications, as by its use satisfactory results are more readily obtained, and special precautions are less often required. Smith[427] used *n*-butyl alcohol for the analytical separation of sodium and potassium perchlorates. Dakin[428] used butyl alcohol to extract monoamino acids, proline, and peptide anhydrides from the products of hydrolysis of a protein. Monoamino acids are insoluble in dry butyl alcohol, but the extraction actually takes place with water saturated with butyl alcohol and butyl alcohol saturated with water as the two solvent media.

Latschinow[429] found that cholic acid was very soluble in *iso*butyl alcohol, and by the addition of ether he obtained good crystals. Michael *et al*[430] described in detail a method for the preparation of *iso*butyl alcohol in the purest possible condition. Very pure alcohol was fractionated, and a cut of boiling point range 0.15° was taken for purification. Commercial *iso*butyl alcohol often contains traces of a basic substance which cannot be removed by distillation, and the purified alcohol was therefore extracted repeatedly with small quantities of dilute sulfuric acid, washed, and carefully dried. The boric ester of the alcohol was prepared by heating the alcohol with boric anhydride, and was fractionally distilled *in vacuo.* The pure ester was saponified by boiling a short time with aqueous alkali, and the alcohol layer was separated, washed, and dried over lime. The advantage of purifying by means of the boric ester was not alone that the higher boiling point of the ester permitted the removal of all substances distilling at the boiling point of the alcohol but which did not form an ester, but it also permitted a much sharper separation from the higher and lower alcohols which were undoubtedly present to an appreciable extent in all preparations of *iso*butyl alcohol purified by distillation, since the difference in boiling point was increased about three times in the esters. Another advantage of the boric ester was the facility with which it might be saponified; in this respect it had a marked advantage over the benzoate. A letter from Dr. Michael to the author stated that the boric ester method had also been found useful for purifying primary carbinols containing three to seven carbon atoms.

A somewhat similar method for the purification of *n*-butyl alcohol, through the sodium salt of butyl salicylate, was used by Orton and Jones[431]. In this case the purity of the alcohol was determined by observing its critical solution temperature in hydrochloric acid (about 14% by weight) which had been standardized with exceptional care. Lebo[432] removed water and *iso*propyl alcohol from secondary butyl alcohol by fractionally distilling a mixture of the impure butyl alcohol with enough benzene to form a low-boiling binary or ternary mixture with the water and *iso*propyl alcohol present.

Since **amyl alcohol** is more readily available than propyl or butyl alcohols, it is not surprising that more frequent instances of its use are found for special crystallizations, although no general study of its solvent properties appears to have been made. The use of this solvent for crystallization of hemin (from blood) was recommended by Küster[433], and Nencki and Sieber[434] observed that the hemin took 0.25 mole of amyl alcohol of crystallization. The chief use of the alcohol in this connection is for the crystallization of compounds which in other solvents are soluble only with difficulty. Thus Niementowski[435] found that *m*-methyl-*o*-uramidobenzoyl was almost insoluble in most solvents and gave unsatisfactory results when crystallization from other solvents was attempted; when amyl alcohol was used, crystals were readily obtained.

Ulsar and Erdmann[436] pointed out the fact that amyl alcohol possesses marked solvent powers for alkaloids. They prepared morphine and strychnine from powdered drugs by extracting the drug with weak hydrochloric acid, adding ammonia to the extract until the reaction was alkaline, and evaporating to dryness. The residue was extracted with amyl alcohol, which took up both alkaloid and coloring matter; when this extract was shaken with acid the alkaloid was withdrawn, but the color was retained, so that a final shaking of the aqueous layer with a fresh portion of alcohol gave the alkaloid in a comparatively pure state. The use of amyl alcohol as a solvent for the analytical extraction of morphine was recommended by Beal and Hamilton[437], since by the use of this solvent it was possible to obtain the alkaloid in a form suitable for gravimetric estimation. It was found necessary to evaporate the solution in a current of carbon dioxide to prevent oxidation of the morphine.

A particular advantage of amyl alcohol as a solvent for extractions is its high boiling point; not only does this property permit extraction of solids to be carried out at an elevated temperature, but it allows the use of this solvent for shaking out hot or boiling aqueous solutions.

Klingemann and Laycock[438] used amyl alcohol as a solvent for the reduction of tetraphenyl pyrrolone to the corresponding pyrrolidone by the use of sodium. The solution was washed with water, and the alcohol was removed by vacuum distillation. Hammick and Locket[439] found that amyl alcohol as reagent and solvent gave far better yields than ethyl alcohol in the preparation of sodium and potassium phthalimides from phthalimide and the corresponding alcoholate. Hartridge[440] suggested amyl alcohol as a cheap and efficient substitute for absolute ethyl alcohol and clove oil in preparing sections to be mounted for microscopic work or for the microtome.

Various methods have been proposed for the examination of butter and other fats by procedures involving determination of their critical solution temperature in some solvent. Absolute alcohol has been most generally used for this purpose, but possesses the disadvantage of great hygroscopicity. Vandevelde[441] stated that a mixture of about two parts of ordinary (95%) alcohol and one part of amyl alcohol showed the same critical solution temperatures for various fats as did absolute alcohol; in addition to the much smaller tendency of this mixture to take on moisture, it was much more sensitive to traces of impurities in the fats and petroleum oils investigated.

The use by Mylius[442] of **allyl alcohol** for the crystallization of cholic acid is an almost unique case of the use of this solvent. In this instance the product contained one mole of solvent of crystallization.

The properties of **ethylene glycol** as a solvent and a preservative in food and drug technology were discussed by Curme and Young[443] and by Fuller[444].

Glycerol as a Solvent.

Partly because of its importance in pharmacy, the solvent power of **glycerol** has been determined for many inorganic and organic substances (see table III, p. 80). Klever[445] was one of the first workers to publish a table of solubilities in glycerol. Ossendovsky[446] reported the solubilities of a considerable number of compounds purified with special care. Holm[447] made careful determinations of the solubilities of a number of organic and inorganic compounds whose solutions in glycerol are of importance in pharmacy. He found in general that as the strength of the glycerol increased, the solubility of the organic compounds examined also increased, while that of the inorganic compounds decreased. As with other alcohols, there was danger of esterification when organic acids were dissolved; this was found to be the case with tartaric acid. The great variance of results of Ossendovsky and Holm may be due in part to the difference in temperature and strength of solvent, and in some cases to supersaturation in Holm's determinations. To approach equilibrium from both sides he made determinations of the solubilities at 20° both by dissolving in the cold and by dissolving at 90° and cooling to 20° till equilibrium was attained; in the latter case some substances took months to crystallize.

Mariller[448] pointed out that inorganic salts dissolve very slowly in pure glycerol because of the viscosity of the solvent, but that a perfectly anhydrous solution could readily be obtained by triturating the glycerol and a strong aqueous solution of the solute, and distilling off the water under reduced pressure at temperatures below 170°. Some solutions (*e.g.*, 30% potassium carbonate), though perfectly clear, are almost solid at room temperature, though quite fluid when hot.

The utility of glycerol as a solvent for crystallization is limited by its viscosity, but in some cases this disadvantage is more than compensated by the results which may sometimes be obtained by its use. Crude glycocoll containing inorganic salts may be purified, according to a German patent[450], by dissolving in hot, very pure glycerol, and allowing the solution to cool somewhat. The inorganic salts separated as a crust on the walls of the vessel, and the glycocoll-glycerol solution was then drawn off. Several suggestions were given of means of overcoming the difficulty of separating the pure material. The glycerol might be removed by vacuum distillation or steam distillation, or the glycocoll might be precipitated with alcohol; for some purposes the glycerol solution of the glycocoll could be used direct. Erdmann[451] used a mixture of methyl alcohol and glycerol for the crystallization of the nitration product of 1,7-dichloronaphthalene; the increased fluidity of the solvent due to the addition of the alcohol made possible a ready separation of the crystals.

To prevent hydrolysis in the preparation of bismuth benzoate, Godfrin[452] dissolved neutral bismuth nitrate in 50% glycerol and sodium benzoate in 33% glycerol. Both compounds dissolved readily, and when the solutions were mixed and allowed to stand, crystals of neutral bismuth benzoate separated, which were entirely free from the basic salt.

In the preparation of Chloramine Orange[453], glycerol was used as solvent because of its reducing properties. Sodium *p*-nitro-

TABLE III

SOLUBILITIES OF CERTAIN SUBSTANCES IN GLYCEROL

Determinations expressed in grams of solute per hundred grams of carefully purified glycerol. This table is given chiefly because of the difficulty of access to some of the data therein contained; no attempt at completeness has been made.

Substance	Oss	K	Holm[447] (20°)		H & K
	15.0–15.6°	" Room temp."	86.5% glycerol	98.5% glycerol	"Room temp."
NaCl	......	......	......	......	8.2
$NaHCO_3$	8.06	8	......	......	....
Na_2CO_3	98.30	98	......	......	....
Na_3AsO_4	50.00	......	......	......	....
$NaBO_2$	......	......	89.36	111.15	....
Borax	60.00	......	......	......	....
KCl	3.72	......	......	......	7.0
KBr	......	25	......	......	17.7
KI	39.72	40	58.27	50.70	....
KCN	31.84	32	......	......	....
$KClO_3$	3.54	3.5	1.32	1.03	....
K_3AsO_4	50.13	50	......	......	....
NH_4Cl	20.06	20	......	......	10.7
$(NH_4)_2CO_3$	20.00	20	......	......	....
$CuSO_4$	......	30	......	......	....
$CaSO_4$	5.17	......	......	......	....
$BaCl_2$	9.73	10	......	......	....
$ZnCl_2$	49.87	50	......	......	....
ZnI_2	39.78	40	......	......	....
$ZnSO_4$	35.18	35	......	......	....
$HgCl_2$	8.00	7.5	......	......	....
Alum	......	40	......	......	....
$PbSO_4$	30.30	......	......	......	....
$Pb(OAc)_2$	10.00	20	129.3	143.0	....
$FeSO_4$	......	25	......	......	....
Sulfur	0.14	0.1	......	......	....
Phosphorus	0.25	0.2	......	......	....
Iodine	2.00	1.9	......	......	....
H_3BO_3	11.00	10	13.79	24.80	....
Urea	......	50	......	......	....
Oxalic acid	15.10	15	......	......	....
Benzoic acid	10.2	10	1.18	2.0	....
Salicylic acid	......	......	0.985	1.63	....
Tannin	48.83	50	......	......	....
Quinine	0.47	0.5	......	......	....
Quinine sulfate	......	......	0.72	1.32	....

REFERENCES:

Oss = Ossendovsky[446] K = Klever[445] H & K = Herz and Knoch[449].

toluene-*o*-sulfonate was heated with glycerol in the presence of caustic soda. A vigorous reaction took place, in which the glycerol was oxidized by the nitro group of the acid, and condensation resulted — first, of two molecules of the acid with the formation of a stilbene, and subsequently, condensation of two stilbene molecules to give the dyestuff.* In another patent relating to dyestuff manufacture[455], glycerol was proposed as a solvent for the condensation of an amino-azo compound and an aromatic amine to form a blue dyestuff.

Epichlorhydrin, the cyclic ether of α-chloroglycerol, has been used as a solvent, both for simple crystallizations, as, for example, its use by Pawlewski[456] for the crystallization of *p*-nitro diazoaminobenzene, and for the separation of stereoisomers. It was used for this latter purpose by Thiele and Dimroth[457] to accomplish the separation of the *cis*- and *trans*-isomers of dinitrostilbene. The mixture of isomers was readily soluble in the hot solvent, but only the *trans*-isomer separated on cooling. The mother liquor was then evaporated, and the residue, which was mainly *cis*-isomer, but which still contained a little *trans*-, was taken up in ethyl acetate. When to this solution, when cooled, a crystal of the *trans*-isomer was added, rapid crystallization was induced, while the solution remained supersaturated with *cis*-isomer. When crystallization of this form finally began, the liquor was rapidly poured into another container, where the *cis*-form separated in a practically pure condition. Flemming[458] showed that epichlorhydrin possessed the property of dissolving a number of compounds, like copal and hard resins, not soluble in ordinary reagents; it was also found that both epi- and dichlorhydrin were solvents for various nitro compounds, including nitrocellulose and celluloid.

Dichlorhydrin has been suggested[459] as a solvent to extract unsaturated hydrocarbons and other impurities from benzene, petroleum, and petroleum jelly.

Friedburg[460] found that **cyneol**, a terpene isomeric with borneol prepared by Wallach and Brass[461] from *Oleum Cynae,* was an excellent solvent for gum copal.

* For the culmination of extensive researches leading to the establishment of the structure here indicated for this dyestuff, see the work of Green[454].

B. Ethers as Solvents

Ethyl Ether.

Next to alcohol, the most used organic solvent is probably **ethyl ether.** This fact is due to its marked solvent powers, its ready availability, its chemical inertness, and its low boiling point. The advantage offered by the latter characteristic, and which is true to a greater extent with this solvent than with any other of the common organic solvents, is that crystals of precipitates which separate from ether may be readily freed from the solvent by drying at ordinary temperatures; ethereal solutions may be evaporated without heating the solution more than a few degrees above room temperature. For this reason ether is useful in work with compounds which decompose readily, and often such compounds, prepared by the use of another solvent, are finally washed with ether so that the drying may be conducted at a temperature sufficiently low to avoid injury to the unstable product (see page 15). Another extensive use for ether is for extracting aqueous solutions; its limited miscibility with water, combined with its other favorable solvent characteristics, makes its use for this purpose both common and productive of good results.

The requirements of the United States Pharmacopœia[463] state that ether, to bear the mark " U. S. P.", shall contain not less than 95.5% nor more than 97.5% of ethyl oxide [$(C_2H_5)_2O$], the remainder consisting of alcohol containing a little water. Baskerville and Hamor, in their extensive study of ether as an anæsthetic[464], remarked that ether complying with the pharmacopœial requirements might contain as much as 4% of ethyl alcohol, and that generally there were present traces of acetaldehyde, acids, and water; U. S. P. ether would probably not average more than 95% ethyl oxide. The degree of purity necessary for laboratory ether, or ether for analytical purposes, is entirely dependent upon the purpose for which it is to be used. For ordinary reagent uses, the pharmacopœial grade (" Ether for Anæsthesia ") is suitable, and in general may be said to answer all such purposes, but in special cases a more carefully purified ether may be required. The tendency which ether manifests to decompose on standing has been carefully studied by Clover[465], by Rowe[466], and by Rowe and Phelps[408]. Rowe found that out of one hundred samples of anæsthetic ether, thirty-four were badly contaminated.

Purification of Ether.

The customary method of preparing absolute ether consists in shaking the ether repeatedly with water to remove alcohol, and finally drying with metallic sodium. This method was used successfully by Baskerville and Hamor[464], but Lassar-Cohn[467] considered that sodium wire or sodium shavings were not satisfactory, since, on account of the limited surface which they presented, they soon became inactive. He recommended instead the use of the liquid alloy made up of two parts of potassium and one part of sodium; as the water was taken up, the potassium or sodium hydroxide separated as a crust on the sides of the flask, so that the surface of the alloy constantly remained bright. Lassar-Cohn stated elsewhere[468] that potassium, whose reactivity far exceeds that of sodium, might be used in the form of this alloy without the excessive violence of reaction which the pure metal often showed. The alloy might be considered as "diluted potassium," and in all cases the potassium reacted in preference to the sodium. Rowe and Phelps[408] found that the most satisfactory method for purifying ether was that of Taylor and Smith[469], which consisted in shaking the ether repeatedly with strong sulfuric acid, treating with alkaline permanganate solution to oxidize aldehydes, washing with water and acid, drying with calcium chloride, and distilling over sodium ribbon. By drying over sodium, Newman[470] was not able to obtain ether with less than 0.14% of water. Newman developed a method for determining small amounts of water in ether, based on the action of the water present on calcium carbide, and measurement of the acetylene which was evolved.

Durand[471] reported that ether, carefully rectified over sodium, was slowly attacked when boiled with sodium; the liquid sodium-potassium alloy reacted vigorously. These observations are, however, quite at variance with reports of other investigators, and Durand's statement that the products of the reaction are alcoholate and hydrogen must certainly be subject to modification if the reacting compound was ether itself and not a trace of alcohol or water.

Hammond[307] described a method for completely removing water from ether and other organic liquids. Ether vapors were allowed to pass up a column filled with alternate layers of sodium hydroxide and glass beads. Any water vapor present was absorbed by the sodium hydroxide; when ultimately an aqueous solution of sodium hydroxide formed in the drying column, the solution ran out of the bottom of the column into a test-tube suspended within the distilling flask, and was withdrawn from the system. Thus the ether vapors at all times came in contact with a large excess of solid sodium hydroxide in substantially anhydrous condition. Hammond[472] also developed a process for dehydrating ethyl ether in the liquid phase with sodium hydroxide.

Wade and Finnemore[473] made a careful investigation of the various methods which have been proposed for the purification of ether, and concluded that the only method which was capable of giving an entirely pure product was that in which the alcohol was removed by repeated washings with small quantities of water. For 700 g. commercial ether they used 50 cc. portions of water, and only after sixteen washings did the wash water fail to give the iodoform test for alcohol. The washed ether was digested for two days with calcium chloride, rectified over phosphorus pentoxide, and finally fractionated with careful thermometric control; about 75% of the rectified material came over at exactly 34.49°. They found that at 20° one gram of the highly purified ether was capable of dissolving 0.013 g. of water, and remarked that the presence of even a trace of alcohol in the ether markedly increased the solubility of water.

Siebenrock[474] studied the drying effect of salts on ethereal solutions of various compounds. Calcium chloride was not generally satisfactory, owing to its tendency to form compounds with many solutes, and in the same way the use of potassium carbonate was precluded if the solute was capable of saponification. These two salts were best for the drying of pure ether saturated with water; by their use the water content was reduced to about 0.1%. For ethereal solutions for which these salts could not be employed, fused carnallite ($KCl.MgCl_2$) was found to give excellent results when present in considerable excess. Gilman and Beaber[475] reported that an ethereal solution of an alkyl *p*-toluenesulfonate dried with calcium chloride frequently decomposed on distillation, while smooth distillation might generally be ensured by using potassium carbonate as a drying agent. It seemed probable that the potassium carbonate helped by removing sulfonic acid formed by the hydrolysis of the esters. Nef[476] recommended the use of phosphorus pentoxide to remove the last traces of water from ether.

Poleck and Thümmel[477] found that practically every sample of ether that they examined contained an impurity which could not be removed by fractional distillation, but which caused a precipitate in an alkaline solution of mercuric chloride. The impurity, which was found to be vinyl alcohol, was removed by shaking the ether with a mixture of 4.5 parts of saturated potassium bicarbonate solution and one part of saturated mercuric chloride solution; Guérin[478] used mercuric sulfate for the same purpose. According to Lassar-Cohn[467] ether treated in this way is also free from aldehyde, and contains only alcohol and water as impurities. Michaelis[479] proposed a method for the preparation of pure ether which involved refluxing the ether over caustic to remove any impurities present; another method of this type was patented by Flaherty[480].

Van Itallie and van der Zande[481] found that ether contaminated with peroxide gave abnormal solubility results, and tended to explode on distillation. Feist[482] and Herzog[483] showed that even carefully purified ether might become seriously contaminated by material which it extracted from cork stoppers with which it came in contact either during distillation or during storage. On evaporation of one such sample, a crystalline residue of vanillin was obtained.

For a detailed comparison of the many methods proposed for the examination of ether, and for a recommended scheme of analysis, reference may be made to the paper by Baskerville and Hamor previously mentioned[484]. More recently Frankforter and Daniels[485] proposed a very delicate test for the presence of water in ether, based on the fact that anhydrous aluminum chloride will dissolve in anhydrous ether to give a clear solution; the presence of even a trace of water in the ether will cause the formation of a cloud or precipitate. Five or ten cubic centimeters of the ether to be tested were placed in a dry test tube and the tube was closed with a rubber stopper. It was cooled to about 10° by ice or running water, a piece of fresh anhydrous aluminum chloride the size of a kernel of wheat was dropped in, and the tube again stoppered and observed against a black background. As the ether warmed to room temperature a reaction took place, evidenced by the formation of small bubbles which rose to the top of the liquid, carrying with them, in the presence of water, a delicate white cloud which, if present in sufficiently large amount, would spread out as a milky layer near the top of the ether. The test was rendered obscure by the presence of alcohol in amounts larger than about 5%, but so large an amount of alcohol could readily be detected by the evolution of hydrogen upon the addition of metallic sodium. The test was intended to prove the complete dehydration of ether by sodium, and was found delicate enough to detect one drop of water in 500 cc. of ether which had been freshly distilled over sodium. Maass and McIntosh[486] reported that small amounts of water might be detected in ethyl acetate or ether by freezing the liquid and allowing it to melt. Less than 0.03% could be detected as ice crystals in the former liquid, and a smaller amount in ether if alcohol was absent.

To effect complete removal of alcohol, Forbes and Coolidge[487] washed the ether with water until the wash water gave no green coloration on shaking five minutes with strong caustic containing a little permanganate. This was so delicate a test for alcohol that if a drop of alcohol was added to 50 cc. of water in a test tube, the whole poured out, and pure water added, the resulting mixture turned green almost immediately on addition of the reagent.

Rough experiments by Forbes and Coolidge indicated that the presence of 1% of alcohol increased the solubility of ether in water by about 2% of itself; and that of succinic acid in ether by about 20%. Carleton[488] found that the presence of very small amounts of alcohol in ether had a marked influence on the velocity of the reaction between sodium and *iso*amyl bromide. In pure ether this reaction had progressed only about 5% in two hours, while in ether containing 0.05% of alcohol, 85% of the bromide had been acted upon in the same time. Salkowski[489] pointed out the fact that ether containing alcohol was in some cases less apt to form emulsions when used for shaking out aqueous solutions than was pure ether.

The solvent power of ether may also be materially affected by the presence of water, though ether saturated at room temperature contains only a few percent of water. Partheil and Rose[490] observed that while anhydrous ether dissolved only 0.0077% of boric acid, ether saturated with water dissolved 0.188%, and that therefore ether could be used in some cases to extract boric acid from aqueous solutions. Schiff[491] reported that the addition of 1% of water to anhydrous ether increased the solubility of phloretin from about 0.4% to more than 5%. Loeb[492] stated that sodium iodide, which is very soluble in methyl alcohol, was not precipitated therefrom by the addition of a considerable volume of absolute ether, but that wet ether caused an immediate separation of the salt. Voit[493] considered the relative advantages of wet and dry ether for fat determinations. If the solvent contained water, there would be a tendency to dissolve material not soluble in anhydrous ether. Furthermore, if the solid to be extracted was not entirely dry — and in some cases the removal of the last traces of moisture was by no means easy — the ether-soluble constituents might in part be protected by the water from the solvent action of the ether, unless the ether was at the start of the extraction sufficiently dry to take up the water present in the sample. It was accordingly advisable to use carefully dried ether for such determinations. Cusmano and Cattini[494] found that ether saturated with water was a much better medium than dry ether for the oxidation of bucco-camphor by oxygen in the presence of platinum black.

The most common use of ether is as a solvent for the extraction either of fats or of alkaloids; only rarely is it as solvent for a reaction. The outstanding instance of this latter use of ether is in the Grignard reaction: the organomagnesium compound is formed by the action of an ethereal solution of an alkyl halide on metallic magnesium, and to this the second component of the reaction is added, also in ethereal solution. The necessity for using absolutely dry ether in this work is well known.

Another instance of the use of ether as solvent in a reaction was given by Bogert and Hoffman[495], who found that the addition of a few drops of ether from time to time during the diazotization of *m*-nitro-*p*-toluidine materially assisted the reaction by bringing about solution of the diazo body. When ether was used there resulted a perfectly clear purple solution, while in the absence of ether the solution was dark brown, and a considerable amount of the diazonium body remained undissolved as a flocculent precipitate. Perkin[496] used ether in the purification of *o*-dihydroxybenzanthrone; the compound was prepared by the action of glycerol and sulfuric acid on deoxyalizarin, and a concentrated alcoholic extract was poured into a large volume of ether. Tar and impurities were precipitated, and the ether-alcoholic solution contained the benzanthrone in a nearly pure state.

Reactivity of Ether.

While one of the chief advantages of ether as a solvent is its inertness towards reagents, there are cases in which this characteristic does not appear. Jannasch and Bartels[68] found that in the presence of aluminum chloride, ether reacted with benzene, forming hexaethyl benzene, and Jannasch and Rathjen[497] prepared di- and tetraethyl phenol in a similar manner, using an ethereal solution of phenol. The reactivity of ether with acid chlorides in the presence of chlorides of the heavy metals was observed by Descudé[498] and Wedekind and Haussermann[499]. Wedekind[500] reported that a similar reaction took place, to a lesser extent, in the presence of tertiary bases such as pyridine. Berthelot[501] found that ethylbutyl ether was formed when a mixture of diethyl ether and butyl alcohol was distilled over sulfuric acid. A chemical effect of solvent ether less readily explained than the foregoing was noted by Darrah and MacArthur[502]. They stated that ether was not satisfactory for extraction of lecethin from desiccated brain tissue, since when this solvent was used, the lecethin manifested a marked tendency to oxidize; benzene, on the other hand, was quite satisfactory.

Evaporation and Distillation of Ether.

As stated above, ether is particularly well adapted, because of its volatility, for use as a solvent with materials which decompose on heating. This favorable property of ether is not, however, always manifested. Lassar-Cohn[503] stated that ethereal solutions of N-nitraniline[504] could not be evaporated on the water bath because of the instability of the crystals; the ether should be allowed to evaporate spontaneously. In such a case it is probable that favorable results might be obtained by distillation of the ether under reduced pressure, or by evaporation with the assistance of an air blast.

Schär[505] reported the explosion of an ethereal extract during evaporation, and attributed it to the presence in the ether of considerable quantities of hydrogen peroxide. The ether had stood for some years before using. Brühl[506] recommended that ether before distillation should be shaken with a little permanganate, which would rapidly destroy any peroxide present. He did not believe, however, that explosions such as were described by Schär were caused by the presence of peroxide. The inflammability of ether necessitates great care in its evaporation. It goes without saying that an open flame should never be used, and even an electric hot-plate may ignite ether vapors if allowed to become too hot.

The assay of alkaloids or crude drugs by the methods of the United States Pharmacopœia necessitate the use for each assay of several hundred cubic centimeters of ether or ether-chloroform mixture. Instead of discarding after use, or of recovering by distillation, with its ever-present danger of fire, the solvent may be prepared for re-use by repeated extractions with acidulated water, until a test with Mayer's reagent shows absence of alkaloid. Solvent purified in this way may still contain coloring matter, but it will be quite satisfactory for use in alkaloidal assay.

Use of Other Ethers as Solvents.

Dimethyl ether was used with excellent results by Knorr *et al*[507] in their work on the tautomeric forms of acetoacetic ester.

The liquid is very hygroscopic, but has the advantage that it may be evaporated at a low temperature (boiling point −23.7°); solutions in dimethyl ether were maintained at a temperature of −78° by means of a bath of carbon dioxide snow. In work on acetoacetic ester, ethyl ether was not satisfactory as a solvent because of the slight rearrangement of the tautomeric forms of the ester which was always experienced, caused probably by the comparatively high temperature necessary to evaporate the solvent.

Methylal was used by Bourgom[227] as a solvent in reactions involving organomagnesium compounds, and for metatheses with inorganic salts.

Perkin and Robinson[508] found **isoamyl ether** more satisfactory than ethyl ether for the preparation of isoharman, owing probably to its greater solvent power for chloronorisoharman, from which isoharman was prepared by methylation with methyl magnesium iodide.

Anisol (phenyl-methyl ether) was used by Gnehm and Kaufler[509] as a solvent with which to extract bromomethylene violet from a reaction mass; the product was recrystallized from nitrobenzene. Hugounenq[510] found anisol a much better solvent than acetone for the purification of phenyl glucosazone. Zerewitinoff[511] stated that both amyl ether (b. 160°) and anisol (b. 154°) were suitable for use as high-boiling solvents for reactions involving the Grignard reagent.

CHAPTER VI

ORGANIC ACIDS, ESTERS, KETONES, AND BASES AS SOLVENTS

A. Organic Acids as Solvents

Acetic Acid.

Acetic acid as a solvent combines the characteristics, desirable in some cases, of an acid and an organic solvent. While ordinary glacial acetic acid is generally sufficiently pure to use as an anhydrous solvent, its further purification is not a matter of great difficulty. Orton *et al*[512] calculated from the melting point of the acid the amount of water present, and distilled the acid with sufficient phosphorus pentoxide to remove the water by forming phosphoric acid. From two liters of commercial glacial acid, of melting point lower than 16°, the first 50 cc. of distillate were discarded, and the next 1700 cc. melted at 16.4–16.5°. This acid was inert towards chlorine and bromine, and contained only very small amounts of acetic anhydride (0.009–0.04 g. per 100 cc.); the anhydride was readily estimated by shaking the acid with 2,4-dichloroaniline, removing the excess aniline with hydrochloric acid, and determining the anilide as the chloroamine. To remove impurities which reacted with bromine and chlorine, Orton and Bradfield[513] distilled the impure acid from chromium trioxide.

Orton *et al* obtained unsatisfactory results when they attempted to purify the acid by fractional distillation, and found that by fractional freezing a yield of only 10–15% of pure acid could be obtained, but by a combination of these two methods Bousfield and Lowry[514] prepared an acid of melting point even higher than Orton's — 16.60°. They first froze a commercial acid to remove most of the water, then slowly distilled the partially dehydrated product over 2% of its weight of permanganate, using a 12-pear still to retain higher boiling homologues; a single distillation in this way removed all impurities except a little water. The water was removed by fractional freezing: a sample of distilled acid fractionally frozen seven times contained less than 0.0005% of water. They found that acid purified by distillation over phosphorus pentoxide gave a normal conductivity, indicating that all oxidizable impurities had been removed.

Glacial acetic acid has occasionally been used as a menstruum for extractions. Squibb[515] carried out an extensive series of investigations on the use of this solvent instead of alcohol for the extraction of alkaloids from drugs (nux vomica, belladonna, etc.) and obtained favorable results. Willstätter and Bolton[516] found that the most satisfactory method for extracting anthocyanines from petals of various flowers was by macerating the petals for a few days with ten parts of glacial acetic acid and precipitating the anthocyanine acetate with ether.

Glacial acetic acid is of frequent use as a solvent for crystallizations, and occasionally dilute acetic acid serves a similar purpose; Bogert and Hand[517] used 50% acid for the crystallization of acetanthranilic acid, and Schmidt[518] found 80% acid the best medium from which to crystallize phenarsazine oxide. Acetic acid may occur as solvent of crystallization; it is found not infrequently in organic compounds, and Abe[519] reported that sodium acetate on crystallization from glacial acetic acid might under certain conditions take either one or two molecules of the solvent.

It may be necessary to take special precautions to remove the last traces of solvent from a compound crystallized from acetic acid. Johnson and Bailey[520] purified phthalimidobenzylsulfonethylenediamine by crystallization from glacial acetic acid. If the compound was subsequently to be alkylated, it was found advisable to recrystallize from alcohol, as there was a tendency for acetic acid to be occluded; unless this was carefully removed, unsatisfactory results were always obtained on alkylation.

The solvent power of glacial acetic acid for inorganic salts was utilized by Gastalde[521] in the purification of triphenyl pyrylium chloride. The crude material, the reaction product of a Friedel-Crafts condensation in carbon disulfide, was dissolved in glacial acetic acid and filtered. To the clear solution was added a 5% solution of ferric chloride in glacial acetic acid; the ferric chloride addition product of the pyrylium derivative separated quantitatively.

Several investigators have found glacial acetic acid a good solvent for reactions or condensations involving cyanic or hydrocyanic acids. Walther and Hübner[6] prepared phenylamino acetonitriles [R.CH.(CN)NHR′] by dissolving the corresponding aldehyde and amine in glacial acetic acid and adding potassium cyanide in small portions, and Bailey and Pritchett[522] also used acetic acid for a similar purpose. Bailey *et al*[523] showed that in the case of certain weak nitrogen bases, soluble in water only with difficulty, carbamide derivatives were readily formed in glacial acetic acid solution by adding finely ground potassium cyanate; sometimes because of solubility relations and the weak nature of the bases, no reaction could be caused to take place in aqueous solution. In some cases it was advisable to use as solvent a mixture of the acid and chloroform, benzene, or absolute alcohol.

For a quite different type of reaction — the catalytic hydrogenation of phthalimid — Willstätter and Jaquet[524] found glacial acetic acid the best solvent, and its use as a medium in which to carry out oxidations with chromic acid is well known. Lewis and Hamilton[525] prepared dihalogen derivatives of certain organic arsenical compounds by dissolving the compounds in hot glacial acetic acid, refluxing for five minutes with sodium halide, and filtering off the excess salt. As the solution cooled the dihalogen derivatives separated in almost quantitative yields. Underwood and Kochmann[526] used glacial acetic acid as a solvent for the interaction of diphenic acid and acetic anhydride to form diphenic anhydride. Wheeler and Smithey[527] prepared nitrocymene by the action of nitric and sulfuric acids on an emulsion of *p*-cymene in its own weight of concentrated sulfuric acid. During the reaction the temperature was carefully maintained at 0°; to prevent freezing out of nitrocymene, glacial acetic acid (about 15% of the weight of *p*-cymene used) was added to the cymene-sulfuric acid mixture at the beginning of the reaction.

Acetic acid has frequently been used with success for the purification of sugars. In 1882 Wernicke and Pfitzinger[528] patented a process for the crystallization of sugars, based on the ability of acetic acid to dissolve non-sugars, leaving the crystallizable sugar undissolved. The dried raw sugar was treated at a temperature below 70° with 50–70% of its weight of acetic acid (90% or stronger); after forty-eight hours standing the mixture was centrifuged, washed with pure acid, and dried. The acetic acid was recovered by distillation of the mother liquors. Hudson and Sawyer[529] used this method for the recrystallization of mannose, and Hudson and Dale[530] prepared a very pure crystalline glucose in the following manner: A good grade of corn sugar was dissolved in water, decolorized with eponite or norit just below a boil, made just acid to litmus with phosphoric acid, and filtered through an asbestos mat. The colorless filtrate was evaporated under reduced pressure until the solution contained 70–75% of solids, and an equal weight of glacial acetic acid was added. The solution was seeded with crystals of pure glucose and stirred occasionally; crystallization commenced almost immediately, while the solution was still warm. It was found advisable to stir in one more part of acid as the crystallization proceeded, to prevent the formation of a solid mass of crystals. The crystallization was complete in a few hours, or overnight; the thick mass of crystals was filtered, washed with alcohol, and dried. The product, crystallized only once, was better than any "chemically pure" crystalline glucose available on the market. Glacial acetic acid was also found useful for the first crystallization of pure β-glucose; the product obtained by crystallization from a hot concentrated solution in the presence of strong acetic acid contained about 7% α- and 93% β-glucose. The small amount of α-isomer was best removed by crystallization from a concentrated ice-cold aqueous solution by addition of alcohol.

Mangam and Acree[531] made a somewhat different use of acetic acid in the purification of glucose. Their material, which had been crystallized from water, was found to contain a small amount of gummy matter; this was removed by rapidly grinding the crystals in a mortar with small portions of glacial acetic acid, filtering the mass on a Büchner funnel, and washing with alcohol. In this way a product of sharp melting point was obtained. Griffin and Nelson[532] found very advantageous the use of glacial acetic acid for the precipitation of inosite from its hot aqueous solution. By the use of the acid, gums and coloring matter were removed, which was not the case when alcohol was used as a precipitant. The use by Harding[533] of glacial acetic acid as a solvent for the separation of glucose and fructose by successive crystallization may also be mentioned.

Other Aliphatic Acids and Acid Derivatives as Solvents.

While acetic acid has found wide application as a solvent, there are only occasional references to **formic acid** for this purpose. Various methods have been proposed for the preparation of pure anhydrous formic acid. Schlesinger and Calvert[534], by nine distillations of 95% acid from phosphorus pentoxide at 35° and 35 mm., obtained acid of melting point 8.60°, which titrated 99.96%. The acid was partly decomposed by this treatment, and the repeated distillations necessary caused great loss of time. Schlesinger and Martin[535] improved this process by using powdered boric anhydride, made by fusing boric acid; this was allowed to remain in contact with the formic acid for several days. After a few days the powdered material set in a hard mass, from which the supernatant liquid was distilled without bumping at 12–18 mm. and 22–25°. Schierz[536] found that most of the water might be removed from 85% formic acid by warming the acid with the calculated amount of anhydrous oxalic acid and decanting the liquid from the hydrated crystals. The dehydration was completed by the use of boric anhydride. Garner *et al*[537] obtained fairly good results by repeated distillations under reduced pressure with anhydrous copper sulfate as a drying agent, and Boswell and Corman[538] found that 95% acid might be raised to 99.6% by two freezings; the yield was 44%.

Aschan[539] found that concentrated formic acid was the only suitable solvent for the crystallization of α-bromohexahydrobenzoic acid and other mono- and dibromo acids of this series. These acids were soluble in water, alcohol, acetic acid, etc., but separated from these media as uncrystallizable oils. In a subsequent paper[540] Aschan pointed out that formic acid was an excellent solvent for many compounds besides bromocarboxylic acids; its solvent properties were in general similar to those of acetic acid, but its temperature coefficient of solubility was much greater. Because of the lower boiling point of formic acid, it could be evaporated from crystals at a lower temperature, and it possessed to an unusual extent the property of favoring the formation of large crystals. On the other hand, its aldehydic nature [$HCOOH \rightleftharpoons (OH)CHO$] rendered it sensitive to oxidation by inorganic salts of nitric and chromic acids; in only a single instance (that of pinene nitrosochloride) was there action of this kind with an organic compound. Since formic acid is a stronger acid than acetic acid, the danger of esterification of alcohols or phenols was greater. Aschan gave quantitative solubility data for about forty inorganic and fifty organic compounds in 95% formic acid. Inorganic salts were as a rule quite soluble. Compounds like indigo, terephthalic acid, uric acid, and alizarin — commonly considered as difficultly soluble organic compounds — were sufficiently soluble in hot formic acid so that they could be crystallized; the crystals thus obtained were often of good form and size. The use of a mixture of formic and acetic acids was found useful for some purposes.

Oleic acid — like, it seems, almost every other conceivable solvent — has been used in attempts to purify crude anthracene. Remy and Erhart[541] patented a process which consisted in dissolving the raw anthracene in about 1.5 parts of oleic acid or other fatty acid at 110°. The solution was allowed to cool, and the crystals of anthracene were separated by centrifuging. Mabery[542] used **stearic acid** as a cryoscopic solvent for aliphatic hydrocarbons of high molecular weight.

Sulforicinic acid was used by Dubosc[543] as a solvent in the esterification of camphor compounds. In the preparation of these esters, either from camphene or pinene hydrochloride, the slight solubility of the camphor compound in the organic acid used for esterification was found to be a great hindrance. When sulforicinic acid, or other sulfo-conjugated acid, was used together with the acid for esterification, the camphene or pinene hydrochloride dissolved freely, and the esterification was greatly facilitated.

For the study of liquid crystals of azoxyphenetol, azoxyanisol, and anisolazoxyphenetol, Gattermann and Ritschke[544] used

colophony (which is composed chiefly of abietic acid) or hard Canada balsam to crystallize mixtures of the three substances; crystals in these media could subsequently be used for observation under the microscope.

The use of **acetic anhydride** as a reagent or a condensing agent is very common, but few instances have been noted of its use as a solvent. Pure acetic anhydride may be prepared by the method of Walton and Withrow[545]. Tausz[546] found acetic anhydride more satisfactory than sulfur dioxide as a solvent with which to extract aromatic hydrocarbons from petroleum, since the work could be carried out at ordinary temperatures. Dreyfus[547] used acetic anhydride, glacial acetic acid, or mixtures of these liquids as diluents in the reaction between sodium acetate and sodium pyrosulfate to form acetic anhydride. Aguiar and Bayer[548] observed that indigo was soluble in acetic anhydride to which had been added a few drops of concentrated sulfuric acid. Heyl[549] used acetic anhydride as a medium from which to fractionally crystallize the acetates of phytosterols from ragweed pollen. By eight fractionations a very sharp separation was obtained.

The solubility of albumoses and peptones in liquid **formamide** and in fused **acetamide** was noted by Ostromysslensky[550]. The latter solvent was found to take up about 30% of the peptones of egg albumen, but the albumen itself was practically insoluble. Walden[551] pointed out the marked similarity between the solvent powers of formamide and those of water. The two liquids were mutually soluble; both dissolved hydroxyl-containing compounds (alcohols, etc.); both were practically insoluble in benzene, hexane, chloroform, etc.; neither dissolved aromatic hydrocarbons, nitrobenzene, or fats. Both solvents dissolved starch, giving solutions which turned blue with iodine. Formamide manifested amidolysis (analogous to hydrolysis): bismuth and antimony salts gave precipitates of basic compounds when dissolved in formamide. Hydrohalide acids were readily soluble in formamide. Walden purified the formamide which he used by fractional freezing at 0°, followed by fractional vacuum distillation; the material melted at 1.60°.

Ott and Löpmann[552] suggested the use of **malonitrile** as a cryoscopic solvent for compounds, such as cinchonine metaphosphate, for which no other suitable solvent could be found. Germann[553] summarized the investigations which had been carried out of the solvent characteristics of liquid **phosgene.**

Phenols.

Phenol has found application as a solvent in both industrial and scientific work. An English patent[554] has described the use of phenol or its homologues in the purification of crude anthracene; it was stated that if material of 18–25% anthracene content was dissolved in two or three parts of hot phenol, the solution cooled and filtered, and the residue washed with fresh solvent followed with an aqueous solution of an alkali (to remove the phenol), the product contained 50–60% of anthracene, and by a repetition of the crystallization could be brought to a purity of 70% or more. A similar method was recommended[555] for isolating technically pure (80–90%) carbazole from the mother liquors obtained when anthracene is purified by the use of pyridine. Dawson[556] claimed that cresols at their boiling points dissolved about their own weight of anthraquinone; crystals of exceptional purity separated on cooling. The use of this solvent possessed the advantage over aniline or nitrobenzene that the excess solvent could be removed by washing with alkali instead of by more inconvenient drying methods. Atack[557] used phenol monohydrate for the same purpose; this solvent was preferable to pure phenol because it remained liquid at the temperatures (10–25° C.) most favorable to the separation of the purified anthraquinone.

In another case[558] phenol was used as a solvent for impurities present in technical indigo. The powdered dyestuff was heated to 130° with three times its weight of crude carbolic acid or of α-naphthol ethyl ether; after cooling the liquid was filtered and the cake washed with phenol, caustic, and water. The residue consisted of practically pure indigo. Bernthsen[559] used phenol in a somewhat similar way to remove the methylene red which he found as an impurity in methylene blue. Witt[560] crystallized eurhodol by dissolving the base in boiling phenol; to the solution, cooled to 100°, he added boiling alcohol containing a little aniline. The aniline neutralized the hydrochloric acid which was present, and the eurhodol separated in crystal needles.

At the present time crude phenols and cresols are used industrially in this country as solvents in the Brègeat process[561] for recovering alcohol, ether, and other volatile solvents from gas mixtures in which they are present as vapors; this process, described by Roulleux and Dort[562], consists in "scrubbing" the vapor mixture with crude phenol or cresol and subsequently driving off the low-boiling solvent by steam distillation or by heating the liquid from the scrubbers at a temperature below the boiling point of the phenol. Drummond[563] stated that for the recovery of alcohol by scrubbing, cresol possessed no advantages over water as a solvent.

It is not surprising that a compound as reactive as phenol should form addition products, particularly with compounds of basic nature. Moschatos and Tollens[564] found that hexamethyleneamine when crystallized from phenol retained three molecules of the solvent, and Eckenroth[565] experienced considerable difficulty in preparing pure urea by Henschel's reaction[566]: $Ph_2CO_3 + 2\,NH_3 \rightarrow CO(NH_2)_2 + 2PhOH$ because of the difficulty in removing the phenol; the reaction mixture, if allowed to stand, deposited crystals of $CO(NH_2)_2.2PhOH$.

Boessneck and Knoefler[567] prepared *p*-amidophenyloxytrichloroethane by the condensation of chloral hydrate with secondary and tertiary aniline bases, but the yield was so poor that the reaction was not useful commercially. Zierold[568] found, however, that if the reaction was carried out in phenol solution, using anhydrous chloral instead of the hydrate, the yield was almost quantitative. In a modification of Hoffmeister's method[569] for preparing diphenyl ether, use was made by Hirsch[570] of phenol as a solvent for shaking out aqueous solutions. Aniline was diazotized, and the solution was shaken several times with phenol; the diazo compound was found to pass almost entirely into the phenol layer, and if this was drawn off and slowly heated and distilled, a very good yield of diphenyl ether was obtained.

B. Esters and Ketones as Solvents

Esters.

While no extensive use has been made of esters as solvents, in some instances their employment has been found to be of value. Thus Pinner[571] stated that the use of carbon disulfide or chloroform as solvent in the bromination of acetaldehyde gave no satisfactory results, but that when ethyl acetate was used the reaction proceeded smoothly; Matheson[572] suggested ethyl acetate as a reaction medium for the preparation of aldehyde ammonia.

Baskerville and Cohen[573] investigated various solvents for phosgene from the consideration of the industrial use of dissolved phosgene. They stated that the ideal solvent for this purpose should possess the following characteristics: (1) inertness towards phosgene, (2) low vapor pressure, (3) marked solvent powers, (4) ready evolution of the dissolved gas, (5) non-flammability, and (6) cheapness. Ethyl acetate was found to fulfill these requirements excellently, although in points (2) and (6) it was surpassed by benzene.

The presence of a trace of ethyl acetate in another inert solvent was in one case found to improve the conditions of the reaction. Michaelis[574] prepared triphenyl arsine by the action of sodium on an ethereal solution of arsenious chloride and bromobenzene; Phillips[575] substituted chlorobenzene for bromobenzene, and found that the reaction might be stimulated by the addition of a few drops of ethyl acetate. Pope and Turner[576] obtained the best results by the use of chlorobenzene, and as solvent used benzene to which a little ethyl acetate had been added. The yields which they obtained by the three methods were respectively 67%, 71%, and 94%.

Ethyl acetate has frequently been used as a solvent for tannic acid, as in this way a very pure product may be prepared. Etti[577] stated that ethyl acetate used as a solvent for tannins must after distillation from the tannins be washed with sodium carbonate solution and redistilled, since the tannic acid tended to decompose the ester with formation of acetic acid. As the tannin solution was evaporated to dryness, the acetic acid concentration increased and tended to cause partial dehydration of the tannic acid. For this reason it was best to distill off the ethyl acetate under reduced pressure. In their work on the tannins of kola nuts, Knox and Prescott[578] found no acidity in the ethyl acetate after distillation, but carried out the washing and redistillation as a precautionary measure.

Spermaceti (cetyl palmitate) was mentioned by Wartha[579] as being one of the comparatively small number of compounds which are good solvents for indigo.

Aromatic esters have found even less general application as solvents than the aliphatic esters. Riddle[580] reported that **phenyl acetate** was a good solvent for nitrocellulose. **Ethyl benzoate** was used by Brühl[581] as a solvent for the benzoylation of β-methylamidocrotonic anilide. This liquid was used by Gabriel and Leupold[582] as a medium from which to crystallize nitronaphthacene quinone, and by Will[158] for tetranitronaphthalene.

Benzyl benzoate in a general way resembles amyl acetate in its solvent powers. Koehler[583] and Mann[584] reported that benzyl benzoate at 40° dissolved about 20% of its weight of commercial musk; there was no separation of crystals when the solution was cooled. Mann[585] reported that **benzyl cinnamate** at 40° dissolved nearly half its weight of musk.

Aldehydes and Ketones.

Among compounds characterized by the carbonyl group, only the ketones seem to have found any extensive application as solvents. In fact, the only instance noted in which an aliphatic aldehyde was so employed was the use of amylal (valeric aldehyde) by Knoevenagel and Weissgerber[586] for crystallizing benzamarone.

Furfural, until a few years ago a laboratory curiosity, has recently been put on the market as a solvent in commercial quantities. Miner *et al*[587] discussed the chemistry of furfural, and indicated some of its uses as a technical solvent. Its application in rubber analysis was outlined by Dubosc[588], and its use as a biological reagent was discussed by Tharaldsen[589].

Of the ketones, **acetone** has naturally been most generally used, since it is cheap, readily available in a state of purity, sufficiently volatile to be readily driven off by distillation, and possessed of marked solvent powers for many classes of compounds; the miscibility of water and acetone allows modification of solvent powers similar to that attained by diluting alcohol.

A number of methods have been proposed for purifying acetone for use as a solvent. Of these the simplest method, first suggested by St. Gilles[231] and rediscovered forty years later by Sachs[230], is that of boiling the impure material with potassium permanganate; the acetone is not affected, while oxidizable impurities are removed. St. Gilles remarked that acetone from pyroligneous acid was freed from its empyreumatic odor by this treatment.

Shipsey and Werner[590] prepared pure acetone from the technical product by forming an addition product with sodium iodide. They had previously shown[591] that when anhydrous sodium iodide was dissolved in warm acetone, the solution on cooling deposited large crystals of the formula $NaI.3C_3H_6O$; by cooling the solution with ice and salt to $-8°$, the yield of crystals was materially increased. The crystals were drained free from mother liquor, and the acetone was distilled off, dried for twenty-four hours over calcium chloride, and redistilled. Lochte *et al*[592] found that for draining, no filter paper was needed in the Büchner funnel, as the crystals were so large that there was no danger of loss. From commercial acetone, a product was obtained in this way which boiled at 56.1–56.2°, and which gave no test with permanganate even after fifteen minutes. This sample was if anything better than " acetone from bisulfite (Kahlbaum)", and was far easier to prepare than by the bisulfite method. The sodium iodide could be used repeatedly, and as it became hydrated with use, it dissolved more readily in the acetone; 100 g. of anhydrous salt required 440 g. of boiling acetone for solution, while 100 g. $NaI.2H_2O$ dissolved in 100 g. of boiling acetone without saturating the solution. In the first case 27% of the acetone (118 g.) was recovered pure on a single treatment, in the second case 70% (70 g.) was recovered; the quality of the acetone seemed in both cases the same.

A method based on the separation of a constant-boiling mixture of acetone and carbon disulfide at about 39° was proposed by Duclaux and Lanzenberg[593]. The yield which they obtained ranged from 40% to 55% of the total volume of acetone used; methyl alcohol and methylal ($CH_2(OCH_3)_2$) could not be separated from the acetone by this method, since they formed with carbon disulfide a mixture boiling at nearly the same temperature as the acetone mixture.

Frankforter and Cohen[594] reported on the preparation of absolute acetone. After unsatisfactory results with various purifying and drying agents — fractional distillation, calcium chloride, potassium carbonate, and magnesium amalgam — they found that a very pure product could be obtained, even from technical acetone, by drying the material for some time over calcium chloride, decanting the acetone, treating with sodium amalgam, decanting again, and distilling. For simple drying, without other purification, they found that calcium chloride, potassium carbonate, or potassium fluoride gave a completely dehydrated product.

Acetone is commonly used as solvent in the preparation of alkyl iodides from the corresponding chlorides or bromides. This use is based on the fact that sodium iodide is soluble in acetone, while the other sodium halides are insoluble. Tsujimoto[595] based a method for the analysis of fish oils on the ready solubility of the lithium salts of the highly unsaturated acids in acetone which contained 5% of water by volume, and the insolubility or sparing solubility of the salts of saturated or less unsaturated acids in the same solvent.

Kharasch and Chalkley[596] used acetone as a solvent in the mercuration of a phenylammonium salt. They stated that the acetone used should not contain much water, but it must contain a trace. When perfectly dry alcohol and acetone were used, no precipitation of the pure compound took place. On very prolonged standing an impure product separated, probably due to absorption of moisture from the air. When a drop of water was added to the clear solution in dry acetone and alcohol, a precipitate formed; too much water redissolved the precipitate. Mallinckrodt's U. S. P. acetone seemed to contain the optimum amount of water.

Vis[597] pointed out that acetone was suitable for the simultaneous dehydration and de-fatting of proteins such as casein. This operation had previously been carried out in two steps; dehydration with absolute alcohol and de-fatting with ether, but extraction with cold acetone accomplished both purposes. Remler[598] carried out a detailed study of the technical uses of acetone as a solvent. Erdmann[599] used acetone as a precipitant for paraffin from tar, and suggested the use[600] of aqueous acetone containing 25% to 65% of water for extracting phenols from tar.

Gomberg[601] stated that if to a concentrated solution of triphenyl methyl in benzene either ethyl acetate or ether were added, crystalline addition products with the triphenyl methyl were formed, but that if acetone was added, the pure compound separated as a colorless, granular precipitate.

Acetone may sometimes be used as a solvent for a reaction which does not take the desired course when another medium is used. Pucher and Johnson[602] found that when potassium iodide was allowed to act on bromomethylphthalimide in ethyl alcohol solution, the corresponding ether was obtained; when acetone was used, the substitution of iodine for bromine took place smoothly. Varma and Kulkarni[603] reported that in the nitration of *o*- and *p*-cresotinic acids by a mixture of nitrosulfuric and nitric acids, charring might be avoided by the use of acetone as a diluent. On the other hand, it is to be expected that a compound as reactive as acetone should in some cases take part in a reaction for which it is being used as solvent. McMaster and Magill[604] investigated the preparation of ammonium salts of organic acids (glycollic acid was worked with in the case in point) by passing ammonia into an acetone solution of the acid. It was found that if the solution was allowed to heat up, diacetoamine was formed; this difficulty could be avoided by keeping the solution cold, but under these conditions, the ammonia dissolved only slowly. After trying several other solvents, it was found that ethyl acetate was excellent for this work, giving a neutral salt with no formation of by-products.

In occasional instances the use of **higher ketones** has been found advantageous. Lochte[605] purified methylethyl ketone by a sodium iodide process similar to that used by Shipsey and Werner[590] for acetone. Diels and Abderhalden[606] prepared an acid of formula $C_{20}H_{32}O_3$ by the oxidation of cholesterol; the crude acid was obtained as a precipitate mixed with potassium sulfate. This was washed with alcohol and refluxed for half an hour with methylethyl ketone. The potassium sulfate was filtered off, and the solution evaporated to incipient crystallization. Methylethyl ketone was used in a somewhat similar manner by Jacobs and Heidelberger[607] in preparing a compound of hydroquinine and a substituted anilide. The two compounds were boiled in acetone solution, and a gummy mass separated, containing the reaction product. This was boiled with methylethyl ketone, and the gum which separated on cooling was filtered off; on further standing and rubbing the filtrate, colorless crystals of the desired compound were obtained. A further crop of crystals was obtained by boiling the gummy residue with the mother liquor from the first crystallization.

For extraction of the coloring matter from logwood and other dyewoods, Beringer[608] recommended the use of mixtures of ketones boiling higher than 80°. When the extraction was carried out at about 30° these ketones dissolved the dyestuff in a comparatively pure state, whereas acetone extracted more tannin than dyestuff. Crude ketones have also been recommended[609] as solvents for purifying crude anthracene.

Morgan and Lammert prepared pure acetophenone[610] and studied some of its properties as a solvent for sodium iodide[611] and for other alkali halides[612].

C. Organic Bases as Solvents

Of the organic bases only two, aniline and pyridine, have found wide application as solvents; these compounds combine the advantages of ready availability and high-boiling point with an ease of removal from crystals — by washing with dilute acid — which is equalled only by the corresponding property of phenols. A number of other bases, both aliphatic and aromatic, have found more or less application as solvents, due both to their good solvent powers and to their basicity. Scholtz[613] found that many organic bases were excellent solvents for alkaloids, and determined the solubilities of about a dozen alkaloids in aniline, pyridine, piperidine, and diethylamine.

The solvent properties of **liquid methylamine** were carefully investigated by Gibbs[614]. He found that this material was a remarkably good solvent for organic compounds, in this respect exceeding liquid ammonia and perhaps exceeding methyl alcohol, although its advantage over ammonia did not appear to be as great as the advantage of methyl alcohol over water. For inorganic compounds it was not as good a solvent as liquid ammonia, far inferior to water, and ranking perhaps closer to methyl alcohol. Its reactivity with both organic and inorganic compounds was very marked, probably exceeding that of liquid ammonia, the most reactive of the other three solvents mentioned. Next to its marked solvent action, the most striking property of liquid methylamine was its remarkable power of uniting with many substances, both organic and inorganic, as methylamine of crystallization. A more general investigation was carried out by Elsey[615], who made qualitative determinations of the solubilities of about ninety inorganic compounds in one or more of half a dozen aliphatic amines. The simpler primary and secondary amines were shown to be fair solvents at room temperature for many salts; the solubilities decreased with increasing complexity of the solvent. The amines were shown to have high temperature coefficients as solvents; at the temperature of liquid ammonia very few salts were perceptibly soluble in any of the amines.

The application of **aniline** as a solvent seems to have been confined largely to its use as a crystallizing medium, though Holde and Weill[616] suggested aniline saturated with water as a solvent for separating coal-tar oils from mineral oils, and Atack and Anderson[617] used aniline as a high-boiling inert diluent for the caustic fusion of 2-aminoanthraquinone. Bogert and Abrahamson[618] crystallized several thiazole derivatives from aniline, and patents have been granted[619] for the use of this solvent for crystallizing diaminoanthraquinone. In another patent[620] it was claimed that when crude anthraquinone was boiled with aniline and the insoluble portion sucked dry and washed with solvent, a product of purity 99.5% or higher was obtained. In 1875

Schraube[621] pointed out the tendency which aniline has for forming addition compounds, and it is probable that the activity which manifested itself in this way has been the chief reason for the comparatively limited use of aniline as a solvent.

Other benzenoid amines have occasionally been used as solvents. In one process[622] for the manufacture of piperazine, one of the intermediates required was the sodium derivative of diacetyl ethylene diamine. This was prepared by dissolving the diacetyl diamine in boiling **dimethyl aniline** and adding the calculated quantity of sodium. After long boiling the sodium completely dissolved, and the desired sodium compound separated; this was filtered from the dimethyl aniline and washed with benzene. Dimethyl aniline was used by Curtius and Ehrhart[623] as a high-boiling solvent in which to carry out the decomposition of benzylazide. Möhlau and Fritzsche[624] used this solvent as a medium from which to crystallize the compound obtained by the interaction of dimethylaniline and *p*-nitroso dimethylaniline.

In an investigation of the rearrangement of diazoamino-*p*-toluene to aminoazo-*p*-toluene in the presence of *p*-toluidine hydrochloride, Nölting and Witt[625] used **p-toluidine**, melted on the water bath, as a solvent. Wieland and Rheinheimer[626] prepared phenarsazine by dissolving its methyl ether in freshly distilled **methyl diphenylamine** and heating the solution to boiling. This solvent was found to serve excellently for the purpose because of its high-boiling point and its inertness towards the reacting substances.

As a solvent, **pyridine** has found a more extensive application than any other organic base. While the chemically pure compound is ordinarily used for this purpose, MacKensie[627] investigated the use of commercial pyridine as an analytical solvent. He found that this material consisted of pyridine, picolines, and water, and possessed a very wide distillation range. More than one-quarter of the material distilled as pyridine hydrate ($C_5H_5N.3H_2O$), which was shown to have a constant boiling point — 94.4°. From the technical material the pyridine fraction came over at 112–118°, and the three isomeric picolines at 135–145°. The hydrate was worthless as a solvent for bitumens, and its presence decreased the solvent power of the pyridine;

the picolines were found to be better solvents for this purpose than pyridine itself.

According to Zerewitinoff[511], all solvents except hydrocarbons, ethers, and tertiary amines either form addition products with the Grignard reagent — methyl magnesium iodide — or react with it, forming methane. Because of the advantages of pyridine as a solvent for reactions of this type, the drying of this liquid has been investigated with considerable care. Wilcox[628] found that a sample of pyridine dried over fused potassium hydroxide (the ordinary method) boiled at 114.5–116.5° (740 mm.). In an attempt to obtain a product of sharper boiling point, a quantity of pyridine was dried over potassium hydroxide for about a month, then was refluxed for six hours over barium oxide (prepared by heating the anhydrous peroxide), refluxed for six hours more over fresh barium oxide, and finally distilled. Two liters of this material distilled with a boiling point range of only 0.35°, which indicated that the product was not only free from water, but also free from homologues. A suggested explanation of the removal of these homologues — which without question were present in the original material, at least in small quantities — was that the slight amount of undecomposed barium peroxide present in the oxide oxidized the homologues to carboxylic acids, which in turn were decomposed by the barium oxide with the formation of pyridine and barium carbonate. Oddo[629] prepared an especially pure material for use with the Grignard reagent by allowing Kahlbaum's pyridine to stand over recently ignited barium oxide, and, after filtration, distilling in the presence of two or three drops of fuming sulfuric acid.

For the determination of hydroxyl groups or water by the action of methyl magnesium iodide on ROH or HOH, with evolution of methane, Zerewitinoff[630] found anhydrous pyridine a very good solvent. He dehydrated the pyridine by allowing it to stand for several days over barium oxide, decanting, and distilling over fresh barium oxide. Pyridine treated in this way evolved no gas on being treated with the Grignard reagent, although great precautions were necessary during the distillation to prevent absorption of moisture from the atmosphere. Tanberg[631] modified the drying method by refluxing the pyridine for twenty-four hours or more over barium oxide, but found that on addition of methyl magnesium iodide considerable quantities of gas were evolved. Zerewitinoff[632] explained this by calling attention to the fact that he and Ostromysslensky[633] had shown that barium oxide possesses reducing properties, so that it seemed possible that the long heating with the oxide to which Tanberg subjected his pyridine caused a partial reduction to some compound like dihydropyridine, which would evolve methane on treatment with the Grignard reagent because of the presence of a labile hydrogen atom. He confirmed the fact, however, that standing over barium oxide, decanting, and distilling over fresh barium oxide gave a pyridine which had practically no effect on the magnesium methyl iodide.

Downs[634] developed a method for removing water from pyridine on an industrial scale, by the addition of sufficient benzene to the wet pyridine to form the constant-boiling mixture whose composition is 10.325 parts of benzene (by weight) to one part of water. Practically all of the water passed over below 80°, so that dry redistilled pyridine could be obtained in a single operation with very little loss. Heap *et al*[635] prepared highly purified pyridine and homologues by recrystallization of the double salts which the bases formed with zinc chloride.

Dehn[636] determined the solubilities of eighty-five organic compounds in pyridine, water, and aqueous pyridine. In the case of solubilities in two pure liquids and in their mixture, there are four possible types of solubility value. The solute may be most soluble in any one of the three solvents used, or it may be less soluble in the mixed solvent than in either of the pure liquids. The system pyridine — water gave rather surprising results in that each of these four cases was observed with a considerable number of solutes. A number of dyes, alkaloids, and other nitrogen-containing compounds were more soluble in the mixed solvent, while certain sugars (lactose, maltose, and raffinose) were less soluble in aqueous pyridine than in either pure solvent. Piettre[637] found that a mixture of equal parts of pyridine and water was a better solvent for humus than was pure pyridine.

A novel use of pyridine as an extraction solvent was made by Cremer[638], who isolated phlorizin from urine by shaking out with a mixture of pyridine and ether. Pyridine was first added to the specimen of urine, and ammonium sulfate added until pyridine began to separate. The extraction was then carried out, and the phlorizin obtained by evaporation of the mixed solvents and crystallization from chloroform. In attempts to purify oak tannin, Feist and Bestehorn[639] found that crystals of ellagic acid would separate from a solution of the tannin in pyridine. Accordingly the authors attempted to separate the crystalloid ellagic acid from the colloid tannin by dialysis in hot pyridine. Separation actually took place, but both the acid and the tannin were chemically changed by prolonged heating with the solvent.

Murdoch and Galbraith[640] recommended pyridine as solvent in a process for the use of sodium amalgam to reduce water-insoluble compounds like nitrobenzene or azo derivatives. To the pyridine solution of the compound to be reduced enough water was added to react with the sodium amalgam; the pyridine solution of the reduction product readily separated from the sodium hydroxide solution formed during the reaction.

Pyridine was used with considerable success by Neuberg[641] for the purification of osazones, which dissolved only with difficulty in ordinary solvents, but which were without exception very soluble in pyridine. The high solubilities and the marked tendency to supersaturation rendered purification of small quantities impracticable by crystallization from pure pyridine, but since the addition of a small quantity of pyridine greatly increased the solubility of osazones in all common solvents, by the choice of a proper solvent mixture the crystallization of even very difficultly soluble osazones was readily carried out; the precipitation of a saturated solution of the osazone in pyridine with some indifferent solvent was found to give even better results. It was pointed out that while pyridine, carefully checked for optical inactivity, could be used for polarimetry of osazones, it was necessary to use an asbestos gasket in the polarization tube rather than a rubber gasket, since pyridine exerted a marked solvent action on rubber.

Behrend[642] used pyridine for the preparation of β-glucose from α-glucose; this method was further developed by Mangam and Acree[643]. Crystals of α-glucose were dissolved in about an equal weight of boiling pyridine and allowed to crystallize. The crystals were filtered, washed with ether, and air-dried for a few minutes. They contained one molecule of pyridine of crystallization, which was readily removed by heating for half an hour at 105°, followed by desiccation over sulfuric acid. The resulting product was β-glucose in 68% yield and of good purity.

Pyridine was used by Adams and Gilman[644] as a medium in which to carry out the reaction between oxalyl chloride and phenol; the reaction when carried out without solvent gave very poor results, due chiefly to the volatility of the chloride. About two grams of pyridine were cooled well in ice, and to this five grams of pure oxalyl chloride were added slowly. The addition product of the two substances separated instantly in the form of yellow lumps, which were carefully crushed before proceeding. Two moles of phenol were dissolved in a little pyridine, and this solution was gradually added to the oxalyl chloride-pyridine compound; the mixture was allowed to stand for two hours at a temperature not exceeding 0°. To obtain the ester, the reaction mixture was poured into a mixture of concentrated hydrochloric acid and ice; the pyridine went into solution, and the ester precipitated.

Verley and Bölsing[645] found that pyridine was an excellent medium for the esterification of alcohols or phenols with acetic anhydride; the reaction went smoothly, without by-products, and was in many cases almost quantitative. These favorable results were explained by the fact that the reaction proceeded according to the following equation:

$$\mathrm{R.OH + Ac_2O + Py \rightarrow R.OAc + Py.AcOH}$$

In this way there was no danger of hydrolysis of the ester by the free acid formed during the esterification. The neutralizing action of pyridine in reactions in which acids are formed is one of the very few instances in which chemical action of the solvent is beneficial to the course of the reaction, but the basic character of pyridine which gives rise to this effect is in many cases the chief advantage which this solvent has as a reaction medium in preference to the more generally used liquids.

The general availability of pyridine as a solvent for organic sulfur compounds was questioned by Raffo and Rossi[646]. They found that when sulfur was boiled with pyridine a distinct action took place with evolution of hydrogen sulfide and formation of tar; when organic sulfur derivatives were boiled with pyridine there was also evolution of hydrogen sulfide. In this case it seemed probable that, to some extent at least, the pyridine acted as a catalyst to favor decomposition of the solute, since certain additive reactions of nitriles and hydrogen sulfide were reversed in boiling pyridine. Mannessier[647], however, used pyridine successfully in separating dithiosulfindene from thiosaccharin. The mixture of these two compounds, prepared by heating saccharin with phosphorus pentasulfide, was dissolved in cold pyridine; on addition of water the dithiosulfindene was precipitated, while the thiosaccharin remained in solution.

Raw pyridine bases have been used industrially as solvents for purifying certain compounds. By one process[648] crude indigo from the phenylglycine process was boiled with pyridine bases; these, it was claimed, removed the impurities and left pure indigo. A method for purifying anthracene[649] was based on the fact that carbazole was much more soluble in pyridine than was anthracene, and for that reason anthracene containing much carbazole could be greatly increased in purity by crystallization from pyridine. According to the patent specifications, crude material containing 33% anthracene, when crystallized from 1.75 parts of raw pyridine bases, gave a product of 82.5% anthracene content.

Quinoline has found little use as a solvent. Walton and Lewis[650], in their work on the partition coefficient of hydrogen peroxide between water and various organic solvents, made the interesting observation that the coefficient for quinoline was less than one. In other words, when quinoline was agitated with an equal volume of aqueous peroxide solution, it removed more than half the peroxide from the water; at 0° with certain concentrations, the quinoline was found capable of removing nearly 80% of the peroxide. Scholl and Berblinger[651] stated that indanthrene, which was almost insoluble in most organic solvents, could be dissolved in five hundred parts of boiling quinoline; when the solution was cooled the indanthrene separated in blue needles like indigo. A 1% alcoholic solution of quinoline was used by Hüfner and Otto[652] for crystallizing oxyhemoglobin from the blood of swine.

By the specifications of a German patent[653], **quinaldine** (methylquinoline) was used as a medium from which to crystallize the condensation product of *p*-nitroso dimethylaniline and β-naphthoquinone sulfonic acid.

CHAPTER VII

HYDROCARBONS AS SOLVENTS

A. Aliphatic Hydrocarbons

The most distinctive characteristic of aliphatic hydrocarbons is their almost total lack of chemical reactivity; it is because of this quality that they received the name of **paraffins** (from *para-affinatus*). Since one of the chief requirements of a solvent is that it should be inert towards solutes under as wide as possible a range of conditions, it might be expected that aliphatic hydrocarbons would have found very general application for solvent purposes. That this has not been the case is due largely to the very limited solvent powers of the paraffins: practically no inorganic compounds and only a small proportion of organic compounds are sufficiently soluble in hydrocarbons of the aliphatic series to make practicable the use of any mixture of paraffins as a medium for carrying out reactions. It is, however, just this restricted power of solution which makes the aliphatic hydrocarbons as suitable for extracting and crystallizing purposes as they have been found to be. If in a raw material or a reaction product the compound which is sought is soluble in a paraffin solvent, there is greater likelihood of all other contaminating substances being insoluble in such a solvent than in a solvent of any other class.

In the paraffin solvents we encounter practically the only instance of solvents which are mixtures of a considerable number of chemical individuals, and the physical properties of which are dependent primarily on the method of preparation and purification. The various paraffin solvents — petroleum ether, ligroin, gasoline, kerosene, etc. — are obtained as distillation cuts from petroleum, and consequently consist of a mixture of homologues, the relative proportions of which are determined by the particular conditions under which the material was prepared. As Hyde[654] pointed out, there is no definite nomenclature for the various cuts of light petroleum distillate; different authorities are entirely at variance as to just what "petroleum ether" or other specially-named fraction is. The only way to specify accurately the petroleum solvent used in any particular case is to give its specific gravity, or better still its distillation range.

Paraffin solvents prepared for laboratory use are generally sufficiently free from non-paraffins to enable them to be used without further purification. In some cases, however, it has been found necessary to carry out further purification of the solvent. Noelting and Schwartz[655] prepared triquinylmethane by Skraup's reaction, using pararosaniline as the amine; the crude product was extracted with ligroin which had been shaken with concentrated sulfuric acid and distilled. With the commercial solvent without further purification only tar was obtained by the extraction. Remsen and McKee[656] found that ligroin b. 90–125° was the best solvent for crystallizing the dichloride of *p*-sulfobenzoic acid, but with the commercial solvent colorless crystals could not be obtained. The ligroin was purified by shaking with concentrated sulfuric acid until it almost ceased to color the acid, washing with hot water, then with hot dilute sodium hydroxide solution, and finally with water again until free from alkali. After drying over calcium chloride and filtering, the solvent was ready for use. For extracting the ethereal oils from flower petals, petroleum ether of sp. gr. 0.650 was found[657] to be the best of the various volatile solvents investigated. The solvent for this purpose was carefully washed with concentrated sulfuric acid, sodium carbonate solution, and water, and then was redistilled.

Another possible disadvantage of unpurified petroleum solvents was observed by Marshall[658]. When the 20–50° fraction obtained by the redistillation of commercial petroleum ether was allowed to stand in a stoppered, partly filled flask exposed to the sunlight, a small amount of residue non-volatile at 100° was obtained; in one case 200 cc. of solvent after thirty days gave 0.0072 g. of residue. In some kinds of work even this small amount of residue might be undesirable, so that for such work it would seem safer to redistil the solvent immediately before using.

For various reasons it may be desirable to use paraffin solvents of a limited and predetermined boiling point range. Liebermann[659] used petroleum ether to extract one component from a mixture of acids from cocaine alkaloids. By spontaneous evaporation of this solution, the acid sought was obtained in glassy crystals. In order to be sure of complete evaporation of the petroleum solvent at ordinary temperatures, only that fraction of the solvent was used which distilled at 60–70° on the water bath. For crystallizing the dibromide of angelic acid, Wislicenus[660] used a mixture of pentanes boiling at 33–39° which he obtained by repeated fractionation of petroleum ether. This solvent dissolved about twice its weight of the dibromide, and by cooling with ice water, the dibromide was caused to crystallize out. According to Tiemann and Krüger[661], ligroin of boiling point range 60–80° was well suited as a crystallizing medium for dimethyl homophthalimide; a lower boiling ligroin could not be used because of the limited solubility of the amide. Auwers and Hüttenes[662] found that by boiling with ligroin of boiling point 120–130°, 3-phenyl indazole of melting point 115–6° could be changed to the isomer melting at 107–8°.

Castille and Henri[413] found several advantages in the use of the hexane fraction from petroleum ether, boiling at 65–70°, as solvent. No addition compounds were formed; solutes were in the normal molecular state most like that of their vapor; unstable compounds remained unchanged in hexane solution longer than in any other solvent or in the pure state; crystals obtained by cooling a hexane solution were remarkable for their purity and their size. The hexane was purified by repeated washings with sulfuric acid monohydrate, followed by washings with alkaline permanganate solution. After drying with sodium and distillation, the solvent was found to be optically pure.

The use of carefully dried ligroin of boiling point 70–90° as solvent for the reduction of triphenyl methyl chloride was recommended by Wieland[663], since a better yield was obtained than with benzene, the customary solvent. Gomberg[664] reported that it was difficult to find solvents from which triphenyl methyl might be crystallized without its taking up solvent of crystallization.

Methyl formate, ethyl formate, and acetone did not give compounds as customarily prepared, but it was probable that these solvents also combined with the hydrocarbon, and that the temperature of dissociation lay very low, below ordinary room temperature. Particularly puzzling was the fact that when petroleum ether was used, the crystals contained petroleum ether of crystallization. Samples of American and of Kahlbaum petroleum ether, thoroughly washed with nitric acid and then with permanganate, still combined with triphenyl methyl to give crystals containing 14–15% of petroleum ether. This point was further investigated by Gomberg and Schoepfle[665], who showed that under proper conditions triphenyl methyl took heptane, cyclohexane, or methyl cyclohexane of crystallization in amounts corresponding fairly closely to the formula $(Ph_3C)_2.X$. With decane, crystals containing varying amounts of solvent were obtained, and were probably mixtures of $(Ph_3C)_2.X$ and $Ph_3C.X$. Jaeger[666] used a mixture of ligroin and ethyl ether as a medium from which to crystallize tri-*p*-chlorotriphenyl carbinol.

Henriques[667] suggested that to bring about solution of fats which were to be saponified in the cold with alcoholic potash an equal volume of petroleum ether be added to the alcohol. In the case of waxes, it was found best to dissolve first in hot petroleum benzine (b. 100–150°), cool, and saponify.

Because of the inertness of the paraffins towards practically all reagents except the halogens, considerations of solubility are in most cases the deciding factors in the use of petroleum solvents. An exception to this rule was pointed out by Hillyer[668], who reported that neither petroleum ether nor pure pentane were suitable solvents for use in the Friedel-Crafts reaction, since both were rapidly decomposed by aluminum chloride at 40–50°.

The higher-boiling petroleum fractions (kerosene, liquid paraffin, etc.) possess the same characteristics of inertness and restricted solvent power that are shown by petroleum ether and ligroin; for that reason their use is particularly appropriate under certain conditions. Read and Prisley[669] used kerosene as a solvent for *iso*butylene in the process which they developed for the preparation of tertiary butyl alcohol by treating *iso*butylene with sulfuric acid at the temperature of the ice-salt bath. The absorption of gaseous *iso*butylene directly by the acid at low temperatures was very slow, so that some inert solvent for the gas was desired. Commercial kerosene, purified by repeated shaking with concentrated sulfuric acid, was found to possess the desired characteristics of good solvent power for *iso*butylene, inertness to cold sulfuric acid, and low molecular weight and freezing point. A procedure almost identical with this had previously been patented by Mann and Williams[670] for commercial preparation of propyl and butyl alcohols from petroleum refinery vapors.

For the preparation of urethanes Weehuizen[671] found that the petroleum fraction boiling between 170° and 200° was an almost ideal solvent. It possessed the advantages (1) that it was anhydrous; (2) that the reacting compounds were readily soluble; and (3) that the products of the various reactions were insoluble, so that a good yield was readily obtained. In the reduction of benzanthrone with dextrine and caustic potash[672], oil with a boiling point of 230°, obtained by steam-distilling kerosene, was used as a diluent. The reaction product, which contained a vatable dyestuff and a non-vatable impurity, was run into a solution of hydrosulfite; the oil formed a protective layer at the top of the solution so that the vatable constituent might be dissolved by the hydrosulfite without being oxidized by air.

An excellent example of the use of liquid paraffin as an inert diluent is found in the method used by Heusler[673] to decompose diazoamino benzene. The compound was suspended in 8–10 parts of liquid paraffin; as the mixture was warmed the diazo compound went into solution, and on further heating decomposed smoothly with gentle evolution of nitrogen. Andreau[674] used paraffin oil of boiling point 250° as diluent in the preparation of glacial acetic acid by the action of concentrated sulfuric acid on sodium acetate. Liquid paraffin was used by Atack and Anderson[617] for the caustic fusion of anthraquinone derivatives at 260–70° C. After the reaction mixture had cooled, the high-boiling oil was removed by washing with petroleum ether. Cone[675] found that by using paraffin (boiling point above 250°) as solvent, it was easily possible to obtain anhydrous sodium naphtholate from technical material· the conversion of this compound to dihydroxy naphtholic acid by treatment with carbon dioxide was readily carried out in paraffin suspension.

The selective solvent action of kerosene was utilized by Harvey and Baekeland[676] for isolating the condensation product of hexamethylene tetramine and carvacrol. An alcoholic solution of the two components was heated for some time and allowed to stand to complete the condensation. The uncrystallized portion was extracted by mixing with kerosene; the precipitate of condensation product was filtered off and recrystallized from alcohol.

Various high-boiling petroleum fractions have been used as crystallizing media. Landauer and Weil[677] used gasoline to crystallize leuco methylene blue; Täuber and Loewenherz[678] isolated *p*-dinitro ditolyl from its resinous condensation product by extraction with high-boiling petroleum, and hot paraffin has been mentioned[679] as a solvent for substituted indigos. Lapworth *et al*[680] used petroleum for the fractional extraction of the essential oil of ginger. The alcohol was evaporated from the alcoholic extract of the root, and the residual oil dried by dissolving in chloroform. The oil from which the chloroform had been evaporated was extracted with hot petroleum, and those portions retained which dissolved freely in the hot solvent, but which redeposited on cooling. After removing all traces of the solvent, the " refined gingerol " was obtained as a viscous, faintly yellow oil.

Since crude petroleum is practically the only commercial source of paraffin hydrocarbons, it naturally follows that, except in special cases, the paraffin solvents which are used are mixtures of a number of homologues. It may in general be said that to prepare a pure hydrocarbon of this class, some synthetic method — *e.g.*, the Wurtz reaction — is necessary, since only by a prolonged and wasteful fractional distillation, as in the work of Young[681] on the isolation of pentanes and hexanes, may one component of a petroleum fraction be separated from its homologues. For solvent purposes the advantages gained by the use of a chemically pure paraffin solvent would be small compared to the difficulty of preparing such a solvent by fractionation, since the desirable properties of these solvents — their chemical inertness and their selective solvent action — are affected very little by the slight change in molecular composition which differentiates isomers and near-lying homologues; any desired boiling-point range is readily obtained by simple distillation.

The only chemically pure aliphatic hydrocarbon that has found any general application as a solvent is **heptane.** Kremers and Sherk[682] reported that *n*-heptane free from isomers might be obtained from the oleoresin of the Diggers pine (*P. sabiniana*); steam distillation of the oleoresin gave about 8% of an oil which was 98% *n*-heptane. This oil was shaken with concentrated sulfuric acid, washed with sodium carbonate solution, and treated with small quantities of permanganate until there was no further decolorization. Several methods were used for the final purification of the hydrocarbon; the most successful was to add about one percent of iodine and to let the mixture stand, with occasional filtering, until no further resin separated. The iodine was then removed by shaking with mercury, and the heptane dried over sodium and filtered; the resulting material possessed a boiling-point range of only a fraction of a degree. In addition to the advantages common to all paraffins of inertness and great selective solvent action, the boiling point of *n*-heptane (98.3°) is very close to that of water. The solubilities of the halogen acids in heptane were very slight.

Purified heptane was used by Leonard[683] as a medium for the preparation of a series of addition products of piperidine with the halides of certain tri- and tetravalent metals. The methods of purification developed by Kremers and Sherk gave a product which was inert towards certain very reactive metallic halides ($AsCl_3$, $SiCl_4$, $SnCl_4$, etc.), though in the presence of even a trace of terpenes or other impurity, a brown resin was formed. Heptane was particularly well suited for use as a solvent in this work not only because of its inertness, but because of the complete miscibility with it of the piperidine and of most of the halides used. Schmidt[518] prepared trianiline arsine hydrochloride by adding aniline to a solution of 18 g. of arsenic trichloride in 100 cc. of heptane. To remove the last traces of the solvent from the crude reaction product, it was necessary to dry the solid at 100° *in vacuo.*

Kremers[684] pointed out the danger of using for accurate work paraffin solvents from chemical supply houses without previous testing. One sample labelled " Hexane for analytical purposes " had a boiling-point range of over thirty degrees; another specimen was labelled " Heptane, boiling point 65–90° " (note that the boiling point of pure heptane is 98.3°). The material possessed a strong odor of benzene, and distillation showed that it was mainly a mixture of benzene and hexane.

Work which has recently been published in connection with vulcanization accelerators indicates that **rubber hydrocarbon** possesses true solvent powers, independent of any chemical action. Several investigators (Skellon[685], Venable and Greene[686], Endres[687], Kelly and Ayers[688]) have studied the solubility of sulfur in rubber — a subject of obvious practical interest because of its importance in the vulcanization process. Bruni[689] heated carefully deresinified rubber hydrocarbon with varying quantities of azobenzene, naphthalene, and *p*-toluidine until the mixture was homogeneous and transparent. The mixture was then slowly cooled, and the temperature noted at which the mixture suddenly became opaque. This temperature was constant for a given mixture, and seemed to indicate that if the mixture was considered as a true solution, the solution was saturated at that point; smooth temperature-solubility curves were plotted. When the solution was maintained for a long time at a temperature above its saturation point, there seemed to be no tendency for the rubber to depolymerize.

Venable and Fuwa[690] showed that rubber had a marked solvent power for various gases, and gave solubility data. That the gases were in true solution and not macroscopically absorbed was proved by the entirely normal effects of variations in pressure and temperature, and the independence of relationship between solubility values and amount of exposed surface. The gases studied — about a dozen in number — divided themselves into three classes: (1) hydrocarbons (methylene and ethane), which naturally were far more soluble in rubber than in water; (2) ammonia and sulfur dioxide, which form hydrates in aqueous solution, and were therefore more soluble in water than in rubber; and (3) other gases (helium, oxygen, hydrogen sulfide, etc.), whose ratio of solubility in rubber to that in water ranged from about 1 to about 2.5. In samples of rubber vulcanized or filled in various ways, the solubility of the gases seemed to be dependent only on the weight of rubber hydrocarbon present.

B. Aromatic Hydrocarbons as Solvents

There are a number of fundamental differences between the aromatic hydrocarbons and the hydrocarbons of the paraffin series. In the preparation of the aromatic hydrocarbons from coal tar there is not the difficulty of obtaining pure compounds that is experienced in the case of petroleum fractions. The " light oil " distillate from crude coal tar consists almost entirely of benzene, toluene, and the three xylenes; because of the technical importance of these three " coal tar crudes," processes have been developed for obtaining benzene and toluene industrially in a high state of purity. No attempt is customarily made to separate the xylenes, which are sold as " solvent naphtha." A difference of much more importance from the standpoint of solvent use is the greater chemical reactivity and the less restricted solvent powers which characterize the benzene hydrocarbons as compared with the petroleum solvents. As has been pointed out, the advantage gained by chemical homogeneity is not a great one, and the other features combine to render the coal tar solvents of distinctly less usefulness than are the petroleum solvents.

Since benzene and toluene are prepared to meet rather exacting commercial standards, the need of special purification is not ordinarily encountered. About thirty years ago Liebermann and Seyewetz[691] pointed out that commercial benzene practically always contained a few tenths of a percent of carbon disulfide. They tested for this by adding a few drops of phenylhydrazine to the benzene, and letting the mixture stand for an hour or so, with occasional shaking. The presence of carbon disulfide in quantities as small as 0.02% was indicated by the formation of a precipitate. Since in the presence of carbon disulfide, side reactions are apt to take place, benzene containing this compound is in many cases not suitable for solvent use. To remove carbon disulfide, Schwalbe[692] recommended that the benzene be boiled with alcoholic ammonia, which Goldberg[693] had shown was better for this purpose than alcoholic potassium hydroxide. The use of a fraction of a percent of ammonia effected complete removal of carbon disulfide, and greatly reduced the amount of thiophene present; after this treatment the benzene was washed with water and distilled. Schwalbe also reported that if nitrogen trioxide was passed into benzene before washing with concentrated sulfuric acid to remove thiophene, this compound was much more easily resinified. Only a little nitrogen trioxide was required; 15 g. of sodium nitrite were sufficient for 1000 g. of benzene, and three shakings with 20 g. of concentrated sulfuric acid gave a thiophene-free product. To remove thiophene, Haller and Michel[694] suggested that the benzene be refluxed for half an hour with 0.5–1.0% of aluminum chloride. Benzene so treated, after washing with sodium carbonate solution and drying, gave negative tests with isatin; the yield was very good. The same procedure might be used for toluene, except that the yield was lower because of effects similar to those encountered in the Friedel-Crafts reaction.

The solvent power of benzene for water is so slight that under ordinary circumstances no special precautions need be taken to dry benzene for solvent use. The increased solubility of silver perchlorate in moist benzene has already been pointed out (page 39), and Farnsteiner[695] reported another case in which the presence of a small amount of moisture made a marked difference in the solvent powers of benzene. Dry barium oleate on warming with dry benzene dissolved not at all, or at most only in traces. The addition of absolute alcohol did not materially affect the solubility of the salt, but if a few percent of 95% alcohol were added to the benzene, the salt dissolved readily, and on cooling, separated in excellent crystals. The addition of a little water to the benzene had the same effect. If only a trace of alcohol was added, a stiff jelly was formed with the oleate, but with more alcohol, the jelly went into solution.

A number of instances have been given (page 16), of the use of benzene to separate organic and inorganic compounds. The insolubility of inorganic salts in benzene was used in rather a different way by Carleton[696], in the titration of sodium bromide which had been obtained as a residue from an organic reaction. The salt was so deeply colored with organic matter that the Mohr method of analysis could not be used, but when the salt was triturated with benzene, the coloring matter dissolved, and on filtering off the benzene, the salt was left ready for analysis.

Benzene of crystallization is frequently found in compounds which have been crystallized from this medium; sometimes the solvent of crystallization is retained with considerable tenacity. Truhlar[697] found that thio-*p*-tolyl urea retained a part of its benzene of crystallization even after it had been heated at 100–110° for four hours. Adams and Gilman[698] reported that the di-β-naphthyl ester of oxalic acid crystallized with one molecule of benzene of crystallization, and that heating at 80–90° did not drive off all of the solvent. By crystallizing from glacial acetic acid, however, the ester was obtained free from solvent, in tiny white needles. Liebermann and Limpach[699] suspected the presence of benzene of crystallization in ψ-tropine, but were not able to prove its presence by loss of weight on heating, since the alkaloid slowly volatilized. By a nitrogen determination it was proved that benzene was absent.

A novel use of the ability which benzene possesses to form molecular compounds was made by Kishner[700] in the preparation of hexahydrobenzene. Benzene was heated to 280° for twenty-four hours with a large excess of strong hydriodic acid; the product was distilled, and came over mostly at 69–73°. The specific gravity of the distillate indicated the presence of unchanged benzene, but this could not be removed by nitration, both because of the incompleteness of the reaction, and because of decrease in yield of the main product. Control experiments with mixtures of benzene and naphtha indicated that benzene might be entirely removed by warming the mixture with triphenyl methane, which on cooling formed a crystalline addition product with the benzene present (see page 17). By two such treatments the hexahydrobenzene was obtained wholly free from benzene.

Benzene was used as an inert solvent in a method for purifying anthracene, which was patented by Wirth[701]. The crude material was suspended in hot benzene, and nitrous gases passed through the solution. The nitrosocarbazol which formed dissolved in the benzene; the residual anthracene was of 75–95% purity. Vignon and Evieux[702], in an investigation of the heats of formation of some organic compounds, found that in benzene solution acetic and benzoic acids so lost their acid properties, and aniline and the toluidines their basic properties, that not only were no salts formed when benzene solutions of the acids and bases were mixed, but that when salts previously prepared were dissolved in benzene, they were decomposed into the component acid and base.

Thiophene, from its similarity to benzene, might be expected to unite with crystals as thiophene of crystallization, and it was shown by Liebermann[703] that this was the case. Both triphenyl methane and dibromo-β-dinaphthyl oxide took one molecule of thiophene of crystallization; the solvent rapidly escaped when the crystals were exposed to the air.

Although the properties of **toluene**, with the exception of its boiling point, are quite similar to those of benzene, this solvent has found but little application in laboratory work. If the solvent is to be used as a medium of crystallization, benzene is generally preferable, since on account of its lower boiling point it may more readily be driven from the crystals; in a reaction if a temperature above the boiling point of benzene is to be attained, xylene would be the natural solvent to use.

Among the few instances of the use of toluene as a laboratory solvent may be cited German patents[704] suggesting toluene as a solvent for phosphorus oxychloride, its use by Heidelberger[705] for crystallizing oxyhemoglobin, by Weiss[706] for crystallizing diphenylguanidine, and the method employed by Staedel[707] for separating the three isomeric dinitro benzophenones by fractional crystallization from toluene. He reported that if even the purest commercial toluene were used or this purpose, the liquor was almost black, and the crystals dark brown. These could be purified by recrystallization from a little glacial acetic acid, but this procedure was wasteful of time and materials. This trouble was almost completely avoided, however, if the toluene used as solvent was first shaken a few times with concentrated hydrochloric acid, then a few times with concentrated sulfuric acid, washed with water, dried, and distilled; this procedure removed pyrrol and thiotolene. Such a solvent gave colorless crystals and almost colorless mother liquors. Gomberg and Sullivan[708] found toluene preferable to either benzene or xylene as solvent in an operation involving the Grignard reagent. Dennis[709] used toluene at 100° to extract β-naphthalene monosulfonic acid from the sulfonation mixture; when the toluene solution was cooled to 5° almost all the sulfonic acid was precipitated.

The chief use of **xylene** as a solvent has been in reductions with metallic sodium. Ruzicka and Trebler[710] prepared homopinocamphoric acid keto ester by boiling the acid diethyl ester with sodium in xylene solution; if benzene was used as solvent, no keto ester was formed. By the method adopted the yield was 10–20% and the authors stated that by the use of a solvent with a boiling point higher than that of xylene, the yield could probably have been increased.

Brühl[711] reported that xylene might be used as solvent in the Grignard reaction. Malmgren[712] found that the action of monobromocamphor on magnesium to form the reagent proceeded very smoothly in xylene, slowly and incompletely in toluene, and not at all in benzene. Tschelinzeff[713] stated that aliphatic hydrocarbons as well as aromatic could be used in the Grignard reaction. McKenzie[714] had little success in the use of the method proposed by Tschelinzeff.

By a recent patent[715] naphthalene might be reduced to tetrahydronaphthalene by slow addition of water to a mixture of naphthalene and metallic sodium in solvent naphtha at 145°. When a mixture of aliphatic hydrocarbons boiling at 115–20° was used in place of solvent naphtha, dihydronaphthalene was formed. For other instances of the use of xylene in reductions with sodium, see the work of Bischoff[716] on methyl malonic ester and of Brühl[717] on borneol.

The fact that " sulfite turpentine " consists largely of ***p*-cymene** renders this compound readily available at a moderate cost. As Wheeler[718] pointed out, cymene is capable of assuming an important position as a solvent, since it is a hydrocarbon of high-boiling point, and in cases where it can be used, is naturally to be preferred to colored solvents like nitrobenzene, or to an ill-smelling solvent like pyridine. The first step in the purification of the sulfite turpentine was the removal of dissolved sulfur dioxide, which was best accomplished by passing a current of air through the liquid. This step was followed by distillation with superheated steam in an apparatus arranged so that the vapors passed through a 30% solution of sodium hydroxide before going into the condenser. The distilled oil was shaken with 5% caustic soda solution and distilled over metallic sodium. Wheeler and Smithey[719] reported that material, even of narrow boiling-point range, prepared by the process outlined above, would turn yellow on long standing, and in a number of other ways would not be entirely satisfactory as a solvent for reactions. This could be prevented by shaking the cymene with a small amount of concentrated sulfuric acid just after the steam distillation. Curtius and Ehrhart[623] found that by the use of xylene as a medium for the decomposition of benzylazide it was not possible to attain sufficiently high temperatures to give a satisfactory product; with *p*-cymene, however, the reaction proceeded without difficulty.

Mesitylene was one of the solvents listed by Zerewitinoff[511] as being suitable as media for reactions at moderately high temperatures in which methyl magnesium iodide was used. Dziewonski[720] used **cumene** as a high-boiling solvent for the isolation of leukacene ($C_{54}H_{32}$) and other heavy hydrocarbons from the product obtained by the pyrogenic distillation of acenaphthene. **Decacyclene** (trinaphthylene benzene) the melting point of which is 402°, was mentioned by Ostromysslensky[721] as being capable of use at very high temperatures; evidence was given of its ability to dissolve about 10% of its weight of graphite.

Naphthalene is practically the only material, solid at ordinary temperatures, which has found important use as a solvent; in certain cases its inertness, its high-boiling point, and its ease of removal by steam distillation have rendered it an ideal reaction medium. The preparation of 1,2-naphthylamine sulfonic acid by rearrangement of naphthionic acid (1,4-naphthylamine sulfonic acid) according to the original patent[722] involved the heating of sodium or potassium naphthionate in a closed kettle, with agitation, to 180–200° until the disappearance of fluorescence of the melt indicated that the reaction was complete. The yields by this method never exceeded 40% and the melt always contained large quantities of by-products and tar. The reason for this was that the powdered naphthionate was a very poor conductor of heat, so that even with the best stirring possible, much of the material was superheated and charred. A patent appearing a few years later[723] modified the method by introducing naphthalene as a solvent. Dry powdered naphthionate was added to two or three times its weight of molten naphthalene in a kettle provided with an agitator and a reflux condenser. The mixture was heated for a few hours to the boiling point of naphthalene (217°); the melt was then cooled, water added, and the naphthalene distilled off with steam. The residue was neutralized with sodium carbonate, boiled, filtered from a little dirt, and the sodium 1-naphthylamine-2-sulfonate precipitated with salt. An almost quantitative yield of acid of high purity was thus obtained.

A similar method was used by Hale and Hoyt[724] for splitting off carbon dioxide from a carbopyrrolic acid to obtain a substituted pyrrol of known structure. Upon heating the acid alone a violent decomposition always ensued; if an equal weight of naphthalene was added to the acid, a smooth decomposition resulted when the mixture was heated in a sealed tube. Erdmann[725] used naphthalene as a solvent in a caustic fusion which formed a part of his process for the preparation of indigo; a similar use of naphthalene was made by Atack and Anderson[617].

The use of **turpentine** (*d*-pinene) as a solvent has occasionally met with success. Linton[726] stated that hot turpentine was an excellent solvent for the asphaltenes and bitumens in asphalt, although in all cases the residue from this extraction contained a small amount of material which was soluble in chloroform. Zwenger[727] used turpentine as a medium from which to crystallize α-cholesterilin.

CHAPTER VIII

INERT LIQUIDS AS SOLVENTS; SOLID DILUENTS

Chlorinated Hydrocarbons.

Halogen substitution products of the hydrocarbons, particularly chlorinated paraffins with one or two carbon atoms, possess certain distinct advantages over the hydrocarbons themselves which have rendered the chlorinated solvents of exceptional usefulness both in the laboratory and in industrial practice. Like the hydrocarbons, both aliphatic and aromatic, the chlorinated solvents are almost entirely immiscible with water, and except in special cases are inert towards organic solutes and inorganic reagents. Unlike the petroleum fractions, to which classification practically all the paraffin solvents belong, the chlorinated solvents used in the laboratory are chemical individuals, and as such are characterized by definite physical properties; recovery of these solvents is not the involuntary fractionation process which inevitably takes place when petroleum solvents are vaporized from a solute or a reaction product. The chlorinated solvents possess a much more general solvent power than do the hydrocarbons from which they are derived, and are, with minor exceptions, entirely non-flammable. This quality is desirable in solvents for laboratory use, and is almost essential for work on an industrial scale. Finally, the chlorinated solvents (and carbon disulfide, which will be discussed later) are the only solvents in general use which are immiscible with water and at the same time heavier than water. This property is of particular value in extractions by the use of the separatory funnel, since the aqueous layer may be allowed to remain in the funnel while several successive portions of solvent are added, shaken, and drawn off.

While chloroform and carbon tetrachloride are by far the most important representatives of this class of solvents, there has been occasional use of the lower chlorination products in work where ready volatility of the solvent was a desideratum. Fischer and Schiebler[728] used ethyl chloride for extraction of β-chloro butyric ester, owing to the volatility of this compound with ether. Henning[729] suggested the use of a mixture of methyl chloride and ethyl chloride to extract resins and perfumes. Since these mono-chlor derivatives do not possess the valuable quality of non-flammability, Henning subsequently[730] recommended a mixture of ethyl chloride (with or without methyl chloride) with about two parts of methyl bromide. The disadvantage of most non-flammable mixtures of solvents is that, while the mixture itself is not flammable, the fact that the mixture is composed of two or more liquids of different boiling points results in the formation either of vapor at the beginning or of residue at the end which is rich in the flammable constituent, so that the advantage of the mixture is largely nullified. Henning claimed that at no time during the volatilization of his chloride-bromide mixture, which boiled at about 8°, did flammable properties exist, either in the liquid or the vapor.

Beckmann[731] used ethylene dibromide as a medium for analytically determining the fat in milk, or for extracting certain constituents of roots and herbs; the ethylene dibromide solution could be used directly for cryoscopic determination of the molecular weight of the solute. Clough and Johns[371] mentioned *iso*propyl chloride as an excellent solvent for fats; the boiling point of this compound, which is readily prepared from *iso*propyl alcohol, is about the same as that of ethyl ether, and there is much less danger from fire. *Iso*butyl chloride and *iso*amyl chloride were also referred to as good solvents for fats and waxes.

The preparation of absolute **chloroform** is not a matter of great difficulty. The following method was proposed by Hantzsch and Hofmann[732]: Shake commercial chloroform for fifteen minutes with concentrated sulfuric acid to remove alcohol, then wash several times with dilute caustic soda, and finally with water; dry over ignited potassium carbonate. They recommended that the purified liquid should not be distilled, but Baskerville and Hamor[733], who made an exhaustive investigation of chloroform for use in anæsthesia, found a final distillation of value; they used as “pure chloroform” only that portion of the distillate coming over below 64°. They also[734] developed tests for a considerable number of the more probable impurities. To detect the presence of water, 20 cc. of chloroform were boiled with one gram of calcium carbide, and the gases which were evolved were passed into ammoniacal silver nitrate solution: a pronounced acetylene test was obtained when the chloroform contained as much as 0.025% of water. To detect alcohol, the chloroform was dried over ignited potassium carbonate if water was present, and was shaken with a lump of caustic potash and a piece of red litmus paper. Anhydrous, alcohol-free chloroform does not dissolve caustic, but traces of either water or alcohol were capable of dissolving enough caustic to affect the litmus paper. Van den Berg[735] purified technical chloroform by shaking with water, then with barium hydroxide solution, drying in dark glass bottles, and distilling on the water-bath in the absence of light. Anschütz[736] prepared pure chloroform by distilling off the solvent of crystallization from salicylid which had been crystallized from technical chloroform; the crystals, of formula $C_{28}H_{16}O_8 + 2\ CHCl_3$, contained about one-third their weight of chloroform of crystallization.

An analytical method for the determination of small amounts of molybdenum in tungsten, developed by Hall[737], was based on the solubility of molybdenum xanthate in chloroform. Peddle and Turner[738] determined the solubility in chloroform of the halogen salts of a considerable number of substituted ammonias. The solubilities of these salts were far greater in chloroform than in any other organic solvent, and the molecular solubilities were but little less in chloroform than in water.

Freudenberg and Peters[739] found chloroform a much more suitable solvent than ether for preparing the addition products of acid chlorides with tertiary amines like pyridine. In addition to the three principal characteristics of an ideal reaction medium — inertness, great solvent power for reacting compounds, and slight solvent power for the reaction product — which chloroform possessed to a greater extent than ether, the authors found that precipitates wet with chloroform were easier to handle than those wet with ether. Odèn[740] used anhydrous chloroform as solvent in the preparation of acyl derivatives of a substituted glucoside.

Inertness towards reagents is one of the most marked properties of chloroform, but in one interesting case chloroform reacted with a solute, and as a result a false identification was made of the product of the main reaction. Gaze[741] stated that the best method for preparing berberin from its sulfate was to form acetone-berberin, by boiling the sulfate with a large excess of aqueous acetone, and to decompose this compound by refluxing for several hours with an alcohol-chloroform mixture. The crystals which separated on cooling he took to be the free base, though he noted that berberin prepared from the sulfate by metathesis with barium hydroxide possessed different properties, notably a far greater sensitiveness towards carbon dioxide. Schmidt[742] had shown that berberin, dissolved in cold chloroform, did not react with the solvent further than to form an addition product, but Gordin and Merrell[743], after showing that Gaze's " berberin base " was actually the hydrochloride, proved that a reaction similar to that between potassium hydroxide and chloroform:

$$4\ KOH + CHCl_3 \rightarrow 3\ KCl + 2\ H_2O + HCOOK$$

took place, with berberin ($C_{20}H_{17}NO_4$) acting as the base:

$4\ B.MeAc + CHCl_3 + 4\ H_2O \rightarrow 3\ B.HCl + B.HCOOH + MeAc + 2\ H_2O$; the berberin formate probably remained entirely in the mother liquor. The fact that this conversion was almost theoretical (86%) indicated that berberin was an unusually strong base; after refluxing for twelve hours with alcohol-chloroform mixture, hydrastin showed no chloride, quinine and morphine only traces, and piperidine, chloride corresponding to about a 10% conversion; a similar reaction was also brought about by phenylhydrazine. It may be noted that berberin crystallized with one molecule of chloroform which was very firmly bound[742]; this product, if dissolved in hot chloroform, took a second molecule of solvent[741]. It seemed probable that these two molecules of solvent were combined in different ways, since one was entirely lost at 100°, while the other was not at all affected at that temperature.

The peculiar solvent or adsorption effect of chloroform-water emulsions was pointed out by Sisley[744]. When a very dilute aqueous solution of a safranine azo dye was shaken gently with chloroform, equilibrium was established in which the dye was divided between the two layers. If the mixture was vigorously shaken, so that the chloroform was emulsified, practically all the dye was removed from the water layer and held in the layer of emulsion. If then the mixture was allowed to stand, the emulsion gradually broke, and the color was given back to the supernatant aqueous layer, so that equilibrium was established as before.

Technical **carbon tetrachloride** is usually prepared by the chlorination of carbon disulfide, so that this compound is the most probable impurity in tetrachloride, as used in the laboratory, though Richardson and Forrest[745] noted the presence of hexachloroethane. Ingold and Powell[746] found it necessary to employ special methods to remove small amounts of chloroform even from tetrachloride of constant boiling point. The purification was carried out either by digesting for several hours with Fehling's solution, or by heating with a strong solution of potassium hydroxide in methyl alcohol. In the use of this latter method the tetrachloride was recovered by adding water and shaking out with ether, and was finally isolated by fractional distillation. Newcomb[747] outlined tests for the purity of carbon tetrachloride.

Carbon tetrachloride shares with chloroform (and to some extent with carbon disulfide) the advantage over all other common solvents of inertness towards the halogens. This solvent has found extensive use industrially as a solvent for oils, fats, and waxes, not only because of its non-flammability and its immiscibility with water[748] but because of the fact that its low latent heat of vaporization cuts down the steam requirements[749]. With particular reference to this solvent, Baskerville and Riederer[750] outlined certain desirable features for commercial extraction media which are almost equally valuable in solvents for laboratory use. In addition to the ability to dissolve freely the substance sought, while leaving unaffected the other material present, the solvent should be free from danger of flammability or explosion. It should be a uniform chemical compound and not a mixture, so that only distillation, and not fractionation, should be required in practice. It should be completely volatile at a fairly low temperature, without imparting any odor to the solute or extracted material. Its vapors when inhaled should not exert any objectionable physiological action. For industrial use, a solvent should not freeze at ordinary winter temperature. Carbon tetrachloride met these requirements excellently, but possessed the disadvantages, compared with the hydrocarbon solvents, of comparatively high cost, and tendency to hydrolyze in the presence of moisture, forming hydrochloric acid which attacked iron apparatus; this latter characteristic is shared by practically all the other chlorinated solvents.

In the laboratory only limited use has been made of carbon tetrachloride as a solvent, though wide mouth bottles of this liquid, colored with a trace of dye to distinguish it from ordinary reagents, are in very general use as a convenient and cheap laboratory fire extinguisher. In the preparation of *o*-nitro benzonitrile from *o*-nitraniline by the Sandmeyer reaction, Friedlander[751] used benzene to extract the nitrile from the copper salts and excess metallic cyanide. Bogert and Hand[752] found boiling carbon tetrachloride more satisfactory for this purpose; since the temperature coefficient of solubility was greater for the nitrile in this solvent than in benzene, the losses in the mother liquor were less. They stated that the use of either solvent was better than recovery by distillation with superheated steam, used by Pinnow and Muller[753].

Snyder[754] pointed out that carbon tetrachloride was capable of extracting fats from crude drugs to as great an extent as petroleum benzine (the solvent recommended by the Pharmacopœia). Unlike the official solvent, it was free from the disadvantages of unpleasant and persistent odor, great flammability, and necessity for the use of special apparatus. Richardson and Forrest[745] used carbon tetrachloride at room temperature to separate natural asphalts from bitumens and other constituents, and Conover and Gibbs[755] found this medium the most satisfactory of several tried for the fractional crystallization of phthalic anhydride. The crude material was dissolved at a temperature just below the boiling point of the solvent, filtered, decolorized with charcoal or fuller's earth, and passed successively through crystallizing tanks at successively lower temperatures. Practically pure phthalic anhydride separated in the first tanks, and impurities almost free from anhydride deposited when the solvent was well cooled.

While mixtures of saturated and unsaturated **chlorination products of acetylene** have found industrial application[756], there does not seem to have been any use of these solvents on a small scale, though Wacker[757] recommended the use of technical dichloroethylene as a laboratory substitute for ether as a solvent. This material, which was a mixture of two isomers, boiled at 50–60°, and had a specific gravity of 1.28. Aside from the entire absence of danger from flammability or explosion, this solvent possessed the advantage of very limited mutual solubility with water, so that the difficulty of drying was much less than with ether, and the loss of solvent hardly appreciable in extraction of aqueous solutions. According to Bodforss[758], trichloroethylene which tended to decompose on standing might be made stable by washing with sulfuric acid. Dangelmajer[759] developed a method for the determination of nicotine by extracting an aqueous solution of the base with trichloroethylene.

Tetrachloroethylene was used by Baddiley *et al*[760] as reaction medium in the sulfonation of α-naphthol by chlorosulfonic acid. Tomiyama and Miyazaki[761] suggested that halogenated ethane or ethylene be used to absorb acetaldehyde or other low-boiling organic compounds produced by synthesis. By this process polymerization of the product was avoided.

Palmer and Adams[762] found **chlorobenzene,** or mixtures of chlorobenzene and alcohol, good media for crystallizing derivatives of phenyl arsine, and Daniels[763] used this solvent to extract benzanthrone from a melt which also contained unchanged anthraquinone, resin, and tar. Mortimer and Murphy[724] prepared pure anthracene and carbazole by repeated crystallizations from chlorobenzene; Lewis[765] purified anthraquinone by extraction with this solvent.

The vat dyestuff obtained by reducing benzanthrone[675] might be purified by extraction with **dichlorobenzene,** which removed non-vatable impurities. Lewis[766] used this solvent for purifying anthraquinone by crystallization.

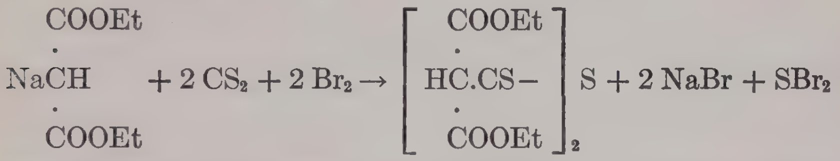
Gomberg and Tabern[767] purified tetraiodofluorescein diacetate by crystallizing from boiling **bromobenzene.** Conant and Sloan[768] used this solvent in work with free radicals, and Gomberg and Schoepfle[769] used both bromobenzene and *p*-bromotoluene. Lehmann[770] used **monobromonaphthalene** as a solvent for various liquid crystals.

Carbon Disulfide.

The most important impurity of **carbon disulfide** is free sulfur; this may readily be removed by the method of Sidot[771] and Arctowski[772]. The carbon disulfide, after a preliminary distillation, was shaken vigorously with mercury until there was no further blackening of the surface of the metal, and until all fetid odor had disappeared; the cloudy liquid was then decanted and distilled. Only small quantities of the disulfide were treated at a time, so that the agitation might be as easy and the state of division of the mercury as great as possible. Arctowski pointed out that carbon disulfide was sensitive to light and to moist air; exposure to either resulted in the ordinary unpleasant odor, and decomposition with the formation of a small amount of nonvolatile matter. Cloëz[773] recommended the use of about 0.5% of corrosive sublimate instead of a much larger quantity of metallic mercury; to the clear liquid from this treatment he added 2% by weight of an odorless fatty body, and distilled the mixture at a moderate temperature on the water bath. A procedure somewhat similar to this last step was used by McKelvy and Simpson[774] for preparing exceptionally pure carbon disulfide from technical material. Twelve liters of the impure liquid were distilled from a flask containing about 900 g. of ceresin; the middle fraction of distillate could not be improved by any further methods of purification. No satisfactory explanation was offered of the mechanism by which the ceresin removed the impurities.

Carbon disulfide was used by Friedburg and Mandel[775] as a solvent for nitrations with nitrogen trioxide. Liquid nitrogen trioxide was prepared by the interaction of arsenious oxide and nitric acid, and was distilled into a receiver cooled in a freezing mixture. Solutions of the trioxide and the compound to be nitrated in carbon disulfide, which had been purified with mercury, were slowly mixed; the low boiling point of the solvent kept down the temperature of the reaction so that resinification and side reactions were minimized.

The usefulness of carbon disulfide as a low-boiling solvent is lessened not only by its flammability and its nauseous odor, but by its instability and its tendency to enter into reaction with solutes. Thus, Voss[776] reported that carbon disulfide partially decomposed into its constituent elements when used for extraction of certain resins, oils, and fats, and Wenzel[777] found that when this solvent was used as a medium for the reaction between bromine and the sodium compound of malonic ester, the reaction took the following course:



$$\begin{array}{c}\text{COOEt}\\ \cdot \\ \text{NaCH}\\ \cdot \\ \text{COOEt}\end{array} + 2\,CS_2 + 2\,Br_2 \rightarrow \left[\begin{array}{c}\text{COOEt}\\ \cdot \\ \text{HC.CS}- \\ \cdot \\ \text{COOEt}\end{array}\right]_2 S + 2\,NaBr + SBr_2$$

When iodine was substituted for bromine, the desired reaction took place smoothly.

The effect of carbon disulfide on the Friedel-Crafts reaction differs according to the reaction substances which are involved. Olivier[778] observed that benzene and *p*-bromobenzene sulfone chloride formed the corresponding sulfone when treated with aluminum chloride in benzene solution, but that when carbon disulfide was used as solvent, the sulfinic acid was formed. If *p*-bromobenzene sulfone bromide and aluminum bromide were mixed in benzene solution there was no reaction, but when disulfide was used, free bromine and a compound of the formula $BrC_6H_4SO_2AlBr_2$ resulted. According to Montagne[779], the Friedel-Crafts synthesis of 4-methoxybenzophenone from *p*-methoxy benzoyl chloride and benzene gave good yields when excess benzene was used as a medium for the reaction, but in the presence of carbon disulfide, only an evil-smelling mass, partially soluble in caustic, was formed.

A very different result was obtained by Wilson and Fuller[780] in work on the Friedel-Crafts synthesis of benzophenone by reaction between benzene and phosgene. When excess benzene was used as solvent, the reaction proceeded normally, but if benzene was added dropwise to a solution of phosgene in carbon disulfide, in the presence of the catalyst, the product was largely benzoic acid. A probable explanation of this was that the reaction took place in two steps, and that the intermediate product ($BzCl.AlCl_3$) which was only slightly soluble in the disulfide, was removed from the sphere of activity before the second step — addition of the second molecule of benzene to form benzophenone — had had time to take place. The intermediate product was isolated, and was shown to give benzoic acid on hydrolysis.

Dimethyl Sulfate.

The chief use of **dimethyl sulfate,** both in the laboratory and the plant, has been as a methylating agent, but a few observations have been made regarding its solvent characteristics. Peachy[781] reported that technical dimethyl sulfate dissolved indigo freely, even in the cold; from this solution the indigo might be completely precipitated by addition of alcohol. When the solution was heated to 100°, chemical action apparently took place, for the blue solution turned brown. Technical dimethyl sulfate always contained a little free sulfuric acid, but the solubility of indigo was apparently not due to sulfonation, since the precipitated dyestuff was entirely insoluble in aqueous alkali. At the same time, the presence of sulfuric acid was important: pure dimethyl sulfate possessed much less solvent power than the technical material, but the addition of a little sulfuric acid, even as little as 0.5%, rendered it a good solvent. Dimethyl sulfate also dissolved various other vat colors to a greater or less extent. According to Mueller[782], the technical dimethyl sulfate encountered in this country is almost chemically pure, and contains no free acid; the dangers attending the use of this compound have been very much exaggerated. Valenta[783] found that dimethyl sulfate dissolved aromatic hydrocarbons but not aliphatic, and made use of this property in identifying high-boiling hydrocarbon residues of petroleum or varnishes. Further work in this field was done by Graefe[784].

Nitrobenzene as a solvent has been used mainly in crystallizations, though Dawson *et al*[785] used this liquid as a medium in which to prepare potassium polyiodides, and Atack and Robertson[786] suggested its use as a solvent in the halogenation of anthraquinone. Atack and Soutar[787] purified a dyestuff by suspending in nitrobenzene, passing chlorine into the suspension, and filtering hot. The impurity (probably a copper salt) was rendered soluble in nitrobenzene by the action of the chlorine. Schönberg and Nedzati[788] found that diacenaphthalene azotide was insoluble in all ordinary solvents, but were able to crystallize this compound without difficulty from nitrobenzene. Vignon[789] and Gabriel[790] used nitrobenzene in a similar way, and Graebe and Philips[791] isolated tri-, tetra-, and pentahydroxy anthraquinoline from the portion of alizarin green insoluble in nitrobenzene. Roberts and Bury[792] studied the use of nitrobenzene as a solvent for cryoscopic measurements. Seidel[793] mentioned **azobenzene** as a solvent for the red dyestuff produced by the oxidation with air of *o*-aminophenol hydrochloride.

Solid Diluents.

While the use of solid diluents has been of service in reactions involving liquids, this procedure has found its chief application when the reaction compounds are solids (or a solid and a gas) and when for some reason it is not practicable to carry out the reaction in solution. The considerations incident to the use of **sand** as a diluent have been thoroughly discussed by McKee and Strauss[794] in a paper on the preparation of benzonitrile by heating together sodium cyanide and sodium benzene sulfonate. The optimum temperature for this reaction was found to be 420–430°; the yield decreased materially as the temperature rose further. An inert diluent was capable of checking the undesirable temperature rise both by its heat capacity and by the improvement which it produced in the thermal conductivity of the mass, which normally was low. A number of runs using 40-mesh sand as a diluent gave yields which attained a maximum with the addition of about 70% of sand. These results indicated that the course of the reaction was influenced by several factors. In the first place, the sand diluted the reaction mixture and lowered the undesired temperature rise, thereby increasing the yield. On the other hand, by dispersing the particles of the reacting materials, the sand rendered contact between them less intimate and thus tended to decrease the yield. The surface of the diluent probably had an effect as well; the benzonitrile vapor on coming in contact with the heated surface of the sand underwent a certain amount of pyrogenic decomposition. With proportions of sand up to 70% the increase in yield due to dilution overbalanced the unfavorable effects of the increase in surface and volume. Above this point, however, these unfavorable characteristics more than offset the beneficial influence of additional dilution, so that the yield diminished. Strauss[795] reported that some forms of crude sodium cyanide contained enough inert impurities to serve in place of the sand as a diluent.

In the preparation of zinc diethyl by the action of ethyl iodide on a zinc-copper couple, Dennis and Hance[796] mixed the pulverized couple with an equal weight of dry sand which had previously been treated with boiling hydrochloric acid. The presence of the sand facilitated the penetration of the powder by the ethyl iodide and thus made it possible to carry out the reaction on a fairly large scale (1 kg. of powder and 500 g. of ethyl iodide) in a single flask.

Windaus and Klänhardt[797] prepared lactones of glutaric acid by heating a mixture of sand and the silver salt of the acid. The proportion of sand used greatly influenced the rate of the reaction: without sand the reaction was vigorous at 80°, while under the conditions found most favorable, the quantity of sand was such that the reaction was complete only after an hour at 150°. In an attempt to prepare cyanogen chloride without the addition of water, Jennings and Scott[798] mixed 50 g. of finely powdered potassium cyanide with an equal bulk of medium fine sand to serve as a heat-distributing medium. This mixture, in a tube 40 × 3 cm., was immersed in a bath at $-5°$, and chlorine was passed through the mass. Numerous scattered areas of decomposition, undoubtedly due to local superheating and excess moisture, indicated that the sand was not able to distribute the heat sufficiently rapidly, so that sand was finally replaced by carbon tetrachloride as a diluent, with very satisfactory results.

For the preparation of allyl iodide by the addition of phosphorus to a mixture of iodine and glycerol, Spenzer[799] recommended that a little ignited sand be placed in the retort. In this way it was possible to overcome the danger of breaking the retort through phosphorus or iodine becoming attached to the bottom, and furthermore the action of the phosphorus was rendered more uniform and regular. Boyd *et al*[800] reduced 3-bromo-1-phenyl cyclohexane in alcoholic solution by the addition of zinc dust mixed with an equal volume of sand.

In an investigation of the action of bromine water on indene, Read and Hurst[801] found that the presence of **kieselguhr** improved the conditions of the reaction, as without this inert diluent there was a tendency for pasty aggregates consisting of the reaction product and unchanged indene to form, preventing isolation of the reaction product.

The insolubility of **sodium chloride** in most organic liquids makes it possible in many cases to use this compound as a solid diluent. When sodium chloride is used in this way for the preparation of compounds insoluble in water, there is the great advantage that the diluent may easily and completely be extracted with water from the reaction product. Such a procedure was used by Wolff[802] for preparing *o*-nitrobenzyl phthalimide from *o*-nitro benzyl chloride and potassium phthalimide. The two components were mixed with 1.5 times their weight of perfectly dry sodium chloride and were heated in a flask on an oil bath. The reaction mixture was extracted with water; the product remained as a yellow powder. In a similar reaction, between ω-chloro-*m*-nitro-*p*-tolunitrile and potassium phthalimide, Banse[803] found that during the condensation, which took place at 120–30°, decomposition could largely be prevented by using dry, finely powdered sodium chloride as a diluent, in the proportion of six parts of salt to one part of each of the reacting compounds. In the preparation of carboxylic acid chlorides by heating a free carboxylic acid with a sulfo chloride[804], alkali chloride, neutral sulfates or pyrosulfates, kaolin, or sand were suggested as diluents.

In the industrial preparation of methyl violet, copper sulfate is used as an oxidizing agent. During the fusion this is reduced to the cuprous state, and in order that re-oxidation may take place it is necessary to keep the melt porous. This was formerly accomplished by the admixture of a large quantity of sand so that the air might have ready access. In a procedure recommended by Creighton[805] the use of sand was entirely replaced by common salt, since this was easily dissolved away from the melt immediately after oxidation. The charge recommended for a batch consisted of 12 kg. of finely ground copper sulfate, 190 kg. of dried sodium chloride, 8 kg. of phenol, and 20 kg. of dimethyl aniline.

CHAPTER IX

SPECIAL MEANS OF INDUCING CRYSTALLIZATION

In the majority of cases no great difficulty is experienced in separating a crystallizable solute from the solvent in which it is dissolved. When a crystallization is to be carried out, the solvent chosen is preferably one in which the solute has a high temperature coefficient of solubility. An almost saturated solution is formed at a temperature near the boiling point of the solvent, the solution is filtered if necessary, with or without the use of a heated funnel, and the clear solution is allowed to cool. It is best to stir the solution while cooling, both to prevent any tendency to supersaturation which may exist, and to cause the formation of small crystals which will filter well and which will occlude but little mother liquor. If the desired solute is the product of a reaction for which the solvent has served as a medium, the choice of solvent should in part depend upon the solubility of the product: the use of a solvent in which the reaction product is insoluble or slightly soluble will not only facilitate the work of preparation, since the product may be separated from the solution by simple filtration, but as a rule the yield will, by the law of mass action, be greater than would be the case if the product remained in solution. While ideal cases of these kinds are the rule rather than the exception, it frequently happens that the solute does not spontaneously crystallize, and in such cases special methods must be used to attain this end.

In addition to the problem of bringing about crystallization in work with compounds which may be obtained in the crystalline form, there must also be considered the purification of amorphous substances. To quote Berdez and Nencki[806], "Purification and determination of empirical formula offer as a rule no great difficulty in the case of crystallizable compounds; this is not the case, however, with compounds which cannot be crystallized, and which do not form simple crystallizable derivatives. With such compounds the criterion of purity must be either the identity of successive portions fractionally precipitated, or the identity of samples purified in various ways."

It is in general true that the greater the molecular weight of a compound, the greater is the difficulty of obtaining the compound in the form of crystals. The explanation of this fact may readily be seen from the elementary theory of crystallization: that crystallization consists in the orienting of molecules of the compound in such a manner that the attractive forces between the molecules may come into play. It is obvious that simple molecules will arrange themselves more readily than will heavier and more complex ones. Because of this fact, it might be inferred that from solvents which cause association, *i.e.*, in which the solute is in the form of aggregates of several molecules, the solute would be less apt to separate in crystals than from non-associating solvents. Pawlewski[807] showed that such was the case. Solutions of carefully purified paraffin in acetic acid gave on cooling distinctly formed crystals, while solutions in benzene, xylene, and chloroform gave only gelatinous precipitates. Cryoscopic determinations indicated that the paraffin possessed an apparent molecular weight of about 360 in acetic acid, and nearly four times that value in concentrated solutions in benzene and xylene. This indicated that the paraffin was in solution in the acetic acid as a crystalloid, and in the other solvents as a colloid, and would explain the inability to form crystals from the hydrocarbon solvents.

Inducing Crystallization by Mechanical Means.

The common practice of inducing crystallization by rubbing the walls of the container with a glass rod was made the subject of study by Fricke[808], who claimed that crystallization under such conditions was due to fine particles of glass rubbed off by the stirring-rod, which served as crystal nuclei. He found that a very moderate amount of rubbing produced enough glass powder to form a distinct precipitate in distilled water. Dede[809] considered that the effect was primarily electrostatic, and stated that even better results were obtained when the rod bore a rubber tip than with a bare glass rod. Fricke[810] admitted the importance of electrical effects, and showed[811] that the particles of glass were negatively charged, but compared the effect of fine particles of glass (those ordinarily produced were so fine that they settled only on standing for hours) to the well-known inoculating effect of dust. He found[812], however, that glass splinters were effective only when they were formed in the presence of the compound which was to be crystallized.

Young[813] investigated various kinds of mechanical stimulus to crystallization. He worked mainly with supercooled water, but confirmed certain of his results by use of supercooled benzene and of supersaturated solutions of salts. The number of degrees of supercooling necessary to bring about crystallization was taken as a measure of the effectiveness of the mechanical stimulus which was applied. Friction between glass and metal was found always to be more effective than friction between glass and glass; copper gave the best results of several metals which were tried. Glass roughened with emery paper gave much better results than smooth glass. Since friction between two solid substances probably consists of a series of small jumps or impacts, it seemed probable that pure impact, without friction, would stimulate crystallization. This was found to be the case, and by experiments with an apparatus similar to a stamp-mill it was found that supercooling was decreased either by increasing the weight of the stamp which was dropped onto the anvil or by increasing the height of fall. By using a stellite hammer weighing 37 grams with a fall of eleven millimeters onto a stellite anvil, Young and Van Sicklen[814] were able to freeze water repeatedly at a temperature slightly under two one-hundredths of one degree below its melting point.

Young and Cross[815] studied the effect of suspended solid particles on the crystallization of a supercooled liquid. They found that crystallization was favored by an increase in the mass of the individual particles or by an increase in the number of particles of a given size, and was hindered by increase in the viscosity of the liquid. Each of these results supported the conclusion that the effect of suspended particles on crystallization is due to the impacts which take place between the particles. The authors pointed out that this hypothesis would explain the fact that the supercooling value may be much increased by filtration, since by filtration small particles are removed from the liquid; various other phenomena incident to crystallization may equally well be explained by the assumption that impacts between suspended particles serve as an important stimulus to crystallization.

Partial Evaporation.

If the temperature coefficient of solubility of the compound sought is small, crystallization cannot be brought about by cooling the solution. In such a case, the solvent may be partially evaporated, and the solute crystallized by concentration. This method was used by Noyes and Potter[816] for crystallizing aminodihydrocampholytic acid, which was no more soluble in hot water than in cold, and which was not soluble in any non-aqueous solvent. Evaporation of the solvent was used for a different reason by Nencki[817] in the preparation of parahemoglobin. This compound was soluble in absolute alcohol which had been saturated at 0° with ammonia, and such a solution was stable indefinitely when kept in a closed container, but in the presence of air the parahemoglobin was readily oxidized to albumen and hematin. If the solution was filtered onto a watch-glass so that the ammoniated alcohol could evaporate rapidly, crystals of the parahemoglobin were obtained contaminated with only a small proportion of the oxidation products.

Herzfeld[818] crystallized maltose from 85% alcohol by evaporating the solvent, but found it advisable to allow the solution first to stand in the cold for a few days in a closed container. The explanation which he gave of the necessity for this preliminary standing was that in the course of its preparation the maltose had become hydrated, and that only after several days in alcoholic solution did it entirely change to the anhydrous form. In the preparation of the acid chloride of a substituted isophthalic acid, Karslake and Bond[819] obtained an oily paste which would not solidify. The crude material was dissolved in carbon tetrachloride, dried with calcium chloride, decolorized with boneblack, and filtered. When the filtrate was allowed to evaporate slowly, the product crystallized in needles.

Supersaturation and Inoculation.

When a liquid or a solution is cooled, it seems to be invariably the case that the temperature must be decreased to a point below the melting point of the liquid or the saturation temperature of the solution before separation of crystals takes place; this phenomenon is known as **supersaturation.** A careful study was made by Young and Burke[820] of the phenomena of solidification exhibited by a large number of identical samples of *p*-nitrotoluene. These were heated and cooled in sealed tubes under various conditions, and the liability and extent of supercooling carefully observed. The time for which a tube had been heated to temperatures above its melting point was of great influence upon the readiness with which it would afterwards solidify, in such a way that the longer the time of heating, the greater the difficulty of bringing about solidification. Thus there seemed to be a sort of sterilization which increased with the time of heating. The higher the temperature to which the tube had been heated, the greater was the degree of sterilization. To a great extent the sterilization was nullified by subsequent solidification, but the reaction, if it be a reaction, which produced the sterilization was not reversible in the liquid state, since the maintaining of the substance in the liquid state at temperatures just above the melting point, after previous treatment at higher temperatures, resulted only in increased sterilization. When the substance was allowed to remain for a long time in the solid state, a degree of sterilization upon subsequent melting was produced that was greater than would have occurred if the time in the solid state had been short.

The phenomenon of supercooling has been recognized for a long time, and it was early observed that crystallization might be brought about without fail by the introduction into the supercooled system of a crystalline fragment, however small, of any solid phase with respect to which the liquid was supercooled; if the liquid was supercooled with respect to more than one solid phase, any one of these might be produced at will by introducing a fragment of the particular phase desired.* This is called crystallization by "seeding" or "inoculation." As long ago as 1854, Williamson[821] wrote: "As regards the preparation of phenol hydrate from the creosote of coal tar, it is observed that the numerous fractional distillations by which it is usually isolated may be abridged by crystallization; for if creosote having a boiling point between 186° and 188° be left for a time in contact with a few crystals of pure hydrate, it deposits a considerable quantity of beautiful colorless needles, which when separated from the mother liquor, distil at 184°, and condense in the neck of the retort in a solid mass of pure phenol hydrate."

---

* See p. 18.

In the preparation of the methyl ester of a phenyl butene acid ester, Davis[822] obtained the desired compound as an oil which in no way could be made to crystallize. A few drops, however, in the bottom of a beaker, finally crystallized in white needles after a month's standing in the corner of the laboratory. With this seed at hand, the preparation of larger amounts was carried out successfully. A similar procedure was used by Gotthelf[823] for obtaining *iso*amyl quinazolone methyl ether in crystalline form. The compound as obtained by evaporating an ethereal solution was an oil which solidified on long standing in a desiccator. The compound was made to crystallize by forming the hydrochloride, dissolving in water, adding a slight excess of sodium carbonate while cooling in ice, and finally inoculating the milky solution with some of the solid ether obtained in the desiccator. Upon standing, small crystalline needles were obtained. Wilson[824] and Dott[825] pointed out that a solution of codeine hydrochloride might remain supersaturated for a considerable time (half an hour or more) even in the presence of a crystal seed.

The use of inoculation to bring about fractional crystallization is exemplified in the method by which Kohler and Smith[826] accomplished the separation of isomers of a certain nitro cyclopropane derivative. The mixture was dissolved in boiling alcohol and the solution carefully guarded against contamination during cooling; the cooled solution was inoculated first with the high-melting and then with the low-melting component.

Under certain conditions homologues of a desired compound may be used as seeds to bring about crystallization. Green[827] reported that pure methylene di-*p*-tolyl triamido toluene separated from solvents in oily drops which would not crystallize. By adding to a petroleum ether solution of the oil a few crystals of the homologous ethylene compound, which had been procured without difficulty, crystals of the methylene derivative were finally obtained. Gomberg and Cone[828] found that triphenyl butane crystallized readily, but triphenyl propane, carefully purified by vacuum distillation, could in no way be made to crystallize. If a little of the oil was seeded with a crystal of the butane derivative, it crystallized readily, and might be recrystallized from methyl alcohol. Once in possession of the crystalline compound, no difficulty was experienced in causing crystallization of fresh lots of oily triphenyl propane, but without inoculation, months' standing would not induce crystallization.

A somewhat different case was that observed by Bell *et al*[829] in regard to the crystallization of *o*-nitro toluene. This compound on cooling crystallized in two forms — metastable (α), melting at $-10.5°$, and stable (β), melting at 4.45°. The former always crystallized first, and frequently remained unchanged for hours, even when the freezing liquid was stirred vigorously. It was found possible to obtain the β-form by cooling the liquid to $-50°$ or $-60°$ in carbon dioxide snow, but a much simpler method consisted in seeding the liquid at about $-10°$ with a few crystals of the eutectic mixture of *o*-nitro toluene and *m*-nitro toluene.

Fractional Freezing.

The use of **fractional freezing** is of particular value in the case of compounds the melting point of which is so low that crystallization is not readily carried out. As its name implies, the process consists either in cooling the liquid until a portion solidifies, or in freezing the entire mass and then allowing partial melting. In either case it is found that the crystals from which the residual liquid has been removed are richer in the higher-melting constituent than was the oil at the start of the operation; it is frequently the case that after a single fractional freezing it is possible to carry out crystallization in the ordinary manner. Bell *et al*[829] found several successive fractional freezings necessary to purify *o*-nitro toluene. The oil was immersed in a freezing mixture until partial freezing had taken place, and the unsolidified portion was decanted from the crystals. The crystals were allowed to melt, and then were frozen again; this process was repeated until the impurities present in the original material were removed and a constant freezing point of −10.5° was reached.

A modification of this method was used by Spenzer[830] in the purification of propylidene-acetic acid, which when pure melted at 7–8°. The crude acid was placed in a flask which was closed with a stopper and a calcium chloride tube; the flask was plunged in a freezing mixture in such a manner that the acid congealed on one side of the flask. The flask was then placed upright in a vessel of ice-water for an hour, and the oil which drained from the crystals was poured off; finally the crystalline cake was itself slightly warmed, so that the last low-melting portions of the acid percolated out.

Thoms[831] isolated an allyl tetramethoxy benzene from parsley oil by freezing the entire mixture in solid carbon dioxide and raising the temperature a few degrees, so that the mass partially liquefied. The mass was then placed on cooled clay, and allowed to stand for twenty-four hours surrounded by a cooling mixture. At the end of that time there remained a considerable residue on the clay which did not melt at room temperature; this residue, crystallized from alcohol, formed colorless plates which melted at 25°. d'Ans and Frey[832] purified organic per-acids by partial freezing and separation of the liquid portion by centrifuging.

Hill and Kelsey[833] found that anhydrous amino-aceto-*p*-chloroanilide could not be crystallized from any solvent, but crystallized from its own melt in slender colorless needles. Middendorp[834] reported that the vacuum distillation of oxymethylfurfurol gave an oil which did not freeze even in carbon dioxide snow, but which formed a vitreous mass when cooled in liquid air. If this was allowed to stand over night in the ice chest it almost entirely crystallized; the small amount of oil which remained was centrifuged off, leaving colorless crystals which melted at 31°. Fractional freezing followed by centrifuging has been suggested for the purification of crude anthracene, both as a method complete in itself, as outlined by Scholvein[835], and as a step utilized in conjunction with further means of purification[836].

Gould[837] suggested an ingenious modification in the purification of naphthalene. By the usual method the crude material containing a considerable percentage of oily impurities is brought to a molten condition and run into shallow pans where it is allowed to crystallize slowly. Thus well-defined crystals are formed, from which the oily impurities are separated by centrifuging, hydraulic pressing, or other means. Gould recommended that the molten crude material, at a temperature slightly above its melting point, be agitated with water or aqueous salt solution at the same temperature, in which the molten material is substantially insoluble. By very slow cooling of the aqueous emulsion, a slurry of naphthalene crystals was formed, from which the oil and the water might be readily and completely removed.

The combination of inoculation and fractional freezing was used successfully by Bourgeois and Dambmann[838] for obtaining a sharp-melting benzaldoxime. By repeated rectifications *in vacuo* a product was obtained which melted unsharply at about 30°. For purification, this product was melted and placed in a water bath at 26–27°. A small crystal of solid benzaldoxime was placed in this liquid, and soon excellent crystals, often of considerable length, were formed in the oily liquid. When about three quarters of the material had solidified, the crystals were rapidly separated from the liquid by suction and pressing with filter paper. By repetition of this process a benzaldoxime was obtained of the desired degree of purity.

Precipitation by Dilution with a Non-Solvent.*

A method of procedure which is in some cases productive of excellent results is to decrease the solubility of the desired compound by the addition to its solution of a liquid, miscible with the solvent, in which the compound is insoluble. Tyrer[839] showed that the solubility of a solute in a mixture of a solvent and a non-solvent is not a linear function of the concentration of the solvent; at the same time, the obvious deduction that solubility will decrease when the solvent is diluted with a non-solvent is in general qualitatively borne out. The question of the optimum concentration of precipitating non-solvent has been considered algebraically by Blackman[840].

---

* See page 28 for instances of precipitation from sulfuric acid solution by dilution with water.

The most frequently used combination of liquids (solvent and non-solvent) for this purpose is that of alcohol and water. This choice is a very natural one: the two liquids are completely miscible, and one is the most generally available solvent for organic compounds, while the other possesses for many organic substances only limited solvent powers. The procedure used in ordinary cases is indicated by the method used by Heidelberger and Jacobs[841] for the purification of a hydrocupreine derivative. The compound was dissolved in a rather large volume of 85% alcohol, and the solution was cautiously diluted with water until the turbidity just redissolved. On standing and rubbing, crystallization slowly started, and was aided from time to time by the careful addition of water. The decrease in solubility of a gas by change of solvents is shown in a lecture experiment devised by Genelin[842]. Ethyl chloride is very soluble in alcohol, but practically insoluble in water. If water is added to a fairly concentrated alcoholic solution of the gas, bubbles of ethyl chloride will be freely evolved. Speyer and Siebert[843] reported that a certain derivative of thebacodeine could be crystallized from water only by the addition of a few drops of alcohol.

Other mixtures of liquids have been used successfully in precipitations of this kind. Ahlqvist[844] recrystallized the ammonium salt of thiocarbaminoglycolic acid from warm ethyl acetate by the addition of chloroform, and Ulpiani[845] dealt with an uncrystallizable ethereal solution in a somewhat similar manner. The solution, which contained certain reduction products of mercuric fulminate, could not be caused to crystallize by cooling, but on the addition of three volumes of gasoline, a precipitate was obtained which, recrystallized a few times from warm water, gave the desired product in a pure state. Gasoline was used as a precipitant by Tingle and Bates[846] to facilitate the purification of 3,6-dichlorophthalic anhydride. The material was prepared by heating the acid in a current of dry air; the crude product was dissolved in benzene and a little gasoline was added. After a few hours a resinous deposit had formed on the sides of the container. The clear liquid was decanted and a little more gasoline was added; this process was repeated until no more resin was precipitated. Addition to the clear liquid of three or four volumes of gasoline brought about precipitation of the dichlorophthalic anhydride as a white powder. For complete purification it was necessary to redissolve the precipitate in a little benzene and repeat the treatment with gasoline.

Mabery[847] removed paraffin from the solid residue of a petroleum distillation by forming a dilute solution of the residue in ether, adding alcohol until flocculent paraffin began to precipitate, cooling and filtering, first at 0° and then at $-20°$. Very little paraffin remained in the oil after the first filtration.

Wheeler and Bost[848] purified *p*-tolylurea by making a hot saturated solution in glacial acetic acid and filtering into cold water. A dense mass of crystals formed, which was filtered off and washed several times with water. The yield was highly satisfactory and the product was pure.

Christiansen[849] purified *p*-nitro-*o*-chlorophenol by suspending the crude material in hot water and gradually adding glacial acetic acid until the solid dissolved completely. As the solution cooled the pure compound separated.

The method of " cold fractionation," used by Charitschoff[850] in the examination of petroleum samples, consisted in dissolving the oil in amyl alcohol and fractionally precipitating portions of increasing solubility by successive additions of small amounts of ethyl alcohol. The portions thus separated were refractionated by precipitating from ether with ethyl alcohol until the specific gravity of each fraction was unchanged by further fractional precipitation. Engler[851] pointed out that constant specific gravity reached in this way was not a criterion of the purity of the product, but indicated merely that a mixture of constituents of equal solubility had been obtained.

The possible usefulness of the addition of a non-solvent to a solution in order to increase the yield is evident. For example, in the preparation of hydroxylamine, Houben[852] increased the yield from 40% of theory to 60% by the use of ether to precipitate the hydroxylamine from alcoholic solution.

The method of precipitation by the addition of a miscible non-solvent, while often capable of yielding excellent results, must in some cases be employed with care. Occasionally the utilization of this method is precluded by its effect on the purity of the compound sought. If impurities present in the solution possess solubility characteristics similar to those of the desired compound, purification by precipitation may be impossible. Ellingson[853] prepared abietic acid by extracting commercial colophony several times with 70% alcohol and repeatedly crystallizing the residue from 95% alcohol; the addition of a few cubic centimeters of acetic acid when crystallizing for the first time seemed to facilitate the crystallization. If water was added to start the precipitation of the acid, the latter separated fairly rapidly, but the compound was not pure, since the crystals occluded an appreciable quantity of resinous matter from the solution. The influence of the rate of addition of the non-solvent was pointed out by Torrey and Brewster[854]. They obtained diphenyl-α-naphthol pyrazoline dissolved in glacial acetic acid as a reaction product. The solute was precipitated by adding small quantities of water at intervals of an hour or more, until no more of the substance separated from the solution. Too rapid addition of water gave a milky liquid, from which it was very difficult to obtain crystalline products.

In the preparation of the beta ester of formylphenylacetic acid, Michael[855] found that the concentration of the sulfuric acid used to precipitate the organic acid from an aqueous solution of its sodium salt had a marked effect on the product. When dilute acid was gradually added, the crystals which slowly separated had a melting point of 60–90°. When acid of specific gravity 1.36 or higher was used, precipitation took place immediately, and a product melting at 95–100° was obtained. The aqueous solution of the sodium salts of the α- and β-isomers had previously been shaken with ether. It was found that unless a current of air was led through the solution to remove the ether before acidification, an oily mixture of the two isomers would be obtained.

Odèn[740] prepared an amorphous form of an acylglucoside by rapid cooling of a hot alcoholic solution and precipitation with water; a crystalline form of the same compound was prepared by slowly cooling a solution saturated at room temperature, with gradual addition of water.

Kharasch and Chalkley[856] found that the addition of ether to an alcoholic solution of a mercurated phenylammonium salt produced only an oil, but that the desired crystalline product might be obtained by allowing the alcoholic solution to stand for twenty-four hours in an empty desiccator beside a beaker of pure ether.

A mixture of solute and non-solute was used by Mabery[847] to separate the high-boiling constituents of petroleum by fractional solution. He found that all the constituents of petroleum dissolved freely in ether, but were quite insoluble in alcohol. By repeated hot extractions with alcohol-ether mixtures of proper concentrations, the residue remaining from vacuum distillation to 300° C. was separated into fractions sufficiently pure for molecular weight determinations.

Overlaying with a Non-Solvent.

A method sometimes available for carrying out very slow precipitations consists in overlaying the solution with the non-solvent or with an immiscible liquid into which may diffuse the solvent component of a mixture of solvent and non-solvent. Graebe and Schultess[857] found that thioxanthone, when precipitated by diluting a solution of the compound in concentrated sulfuric acid, separated in such a finely divided state that it was almost unfilterable. This difficulty was avoided by carefully overlaying the cold solution in concentrated acid with water in such a way that the two liquids mixed only slowly. In the course of twenty-four hours the water had diffused into the acid, and brought about the separation of the thioxanthone as a crystalline product which was readily filtered. This method was used by Gomberg and Britton[858] for the same purpose with excellent results.

Bayer[859] reported that cholic acid might best be crystallized by adding water to an alcoholic solution of the acid until a faint cloudiness was produced, and then overlaying with ether; a similar method was employed by Partheil[860] for crystallizing cytistin hydrobromide. In these cases the mechanism of the process may take either of two courses, depending upon the concentration of the alcoholic solvent. If the concentration of alcohol is so high that ether is readily soluble, the crystallization is brought about by the diffusion of a non-solvent (ether) into the solution, in a manner similar to the precipitation of thioxanthone above cited. If the concentration of alcohol is below 40–50%[861], the ether will no longer be completely miscible, and there will then be involved the diffusion of a portion of the alcohol into the ethereal layer, with consequent decrease in the solvent power of the remaining solvent.

Not so readily explained is the method used by Hufner[862] for the preparation of pure glycocholic acid from the gall of cattle. If the fresh gall was treated with a strong mineral acid, a resinous mass was precipitated, consisting chiefly of glycocholic acid, which had carried down with it some of the more soluble taurocholic acid. If, however, the gall was overlayed with ether before addition of the acid, a crystalline precipitate was obtained which, on a single recrystallization from boiling water, gave colorless crystals of glycocholic acid.

Differential Evaporation.

If it is necessary to add to the solution a considerable quantity of non-solvent to bring about precipitation, it may be possible to induce crystallization by differential evaporation of the solution; this is most readily brought about when the non-solvent is less volatile than the solvent. This method was used by Bosetti[863] for the purification of veratrin. The impure material was dissolved in warm absolute alcohol, and water was added until a faint opalescence was visible. This was dispelled with a little alcohol, and the clear liquid was allowed to evaporate slowly at 50–60°. After a short time considerable quantities of practically pure veratrin separated in the form of crystals. When the solution became cloudy, due to the separation of resinous matter, the liquid was decanted from the crystals, cleared by the addition of alcohol, and subjected to crystallization as before; several crops of nearly pure crystals were thus obtained. Fischer[864] modified this procedure by carrying out the evaporation at room temperature, and found that in this way there was much less trouble from the separation of resins. Jamieson and Wherry[865] crystallized diethylammonium mercuric iodide in a similar manner.

The crude material, from diethylamine and Mayer's reagent, was dissolved in acetone, and chloroform was added in quantity sufficient to produce a slight turbidity. A gentle current of air was directed across the surface of the solution, and crystallization was brought about both by removal of the solvent and by the cooling due to evaporation.

Seidenberg[866] carried out the fractional precipitation of fats and oils by dissolving the material in two or more solvents — generally ether and absolute alcohol — one of which was more volatile and at the same time exerted the greater solvent action on the glycerides. This solvent was slowly removed by aspirating air through the solution; this was accompanied by a considerable decrease in temperature. Due to the cooling and to the gradual removal of the solvent, the various glycerides by degrees came out of solution, in the order of their insolubility in the solvent remaining. To secure a chemically pure product, it was necessary to repeat the fractionation a number of times; the theoretical considerations and the general mode of procedure resembled in many ways the fractional distillation of a liquid. The results, both in yield and in purity of product, were markedly superior to those obtained by fractional crystallization, fractional distillation *in vacuo*, or fractional precipitation by addition of alcohol to ethereal solutions of the fats or oils.

An ingenious modification of the method of differential evaporation was devised by Rümpler[867] for the gradual precipitation of compounds soluble in water but insoluble in alcohol. The compounds were dissolved in water, and alcohol was added until a slight cloudiness was formed; this was filtered off, or dispelled by the addition of a few drops of water. The clear solution was then placed in a desiccator filled with quick-lime instead of with sulfuric acid. The lime removed from the solution the water but not the alcohol; because of the slowness with which this took place, the solute was almost certain to separate in the crystalline form, if such form was capable of existing. This method was successfully used on solutions of arabic acid from gum arabic, peptone from gelatin, and peptone from egg albumen; in the last case by several reprecipitations, crystals several millimeters in length were obtained.

CHAPTER X

SALTING OUT

The "common-ion effect" in solutions of electrolytes is a phenomenon based on displacement of equilibrium in a solution of an ionized compound by addition of a second solute, one ion of which is the same as an ion of the original solute. The solubility product of the original solute, which is a measure of its solubility, is equal to the product of the molal concentrations of the ions which are present in the saturated solution of the solute. It is obvious that since the solubility product is approximately constant for a given solute, any increase in the concentration of one of the ions must be compensated by a decrease in the concentration of the other (assuming that the solute separates into two ions only); such a decrease will result in repression of the ionization of the first solute, and consequent precipitation of it from its saturated solution.

Von Weimarn[868] has summarized the general laws dealing with the common-ion effect. Euler and Lowenhamm[869] showed that the formation of molecular compounds between two solutes in a non-ionizing solvent might result in a mutual increase in solubility instead of the decrease in solubility observed in aqueous solution which is due to the common-ion effect.

The common-ion effect is of comparatively small importance in dealing with solutions of organic compounds, since the effect manifests itself only with slightly soluble compounds, but a phenomenon of an allied type, "salting out," has found very general application. This procedure consists in adding an inorganic salt to the solution of the organic compound, whereby the solubility of the compound is decreased and the compound precipitated; in the case of some sulfur dyestuffs the separation is so complete that the mother liquor of a brown or black dye is absolutely water white, even in comparatively thick layers. No satisfactory explanation has been offered for this effect, which is in no wise dependent on the presence of a common ion, but because of its great importance, both from a laboratory and a technical standpoint, and its interest as a phenomenon difficult to explain, a considerable amount of work has been done to determine the theory which underlies the effect, and the various practical considerations which are involved.

While salting out is not primarily an ionic effect in the same sense as mass action, as is shown by the fact that unionized compounds like ether and alcohol are as generally susceptible to salting out as are ionized compounds, the fundamental laws governing electrolytically dissociated compounds are followed to at least as great an extent as is the case in concentrated solutions of inorganic compounds. Philip[870] and Garner[871] observed that it was theoretically indicated that the solubility of slightly soluble organic acids would markedly increase in the presence of sodium salts of weak acids, due to the establishing of an equilibrium between the hydrogen ion of the slightly soluble acid and the weak acid radical of the sodium salt to form unionized weak acid, so that more of the slightly soluble acid would dissolve to reestablish its own ionization constant. This was shown to be the case, and the magnitude of the influence of the sodium salt was found to be closely related to the strength of the acid from which it was derived. Thus the solubility of benzoic acid ($k = 60 \times 10^{-6}$), which in pure water is soluble 0.29 g. per 100 cc. at 20°, was greater in sodium formate solution ($k_{\mathrm{HCOOH}} = 210 \times 10^{-6}$) than in a sodium salicylate solution ($k_{\text{salicylic acid}} = 1020 \times 10^{-6}$) of the same concentration, and was still greater in the corresponding solution of sodium acetate ($k_{\mathrm{AcOH}} = 18 \times 10^{-6}$). Furthermore, if of two sparingly soluble acids the weaker was also the more soluble, then under the influence of any sodium salt the solubility of the stronger acid was increased to a greater extent than that of the other. The occurrence of this fact, as well as of the main phenomenon, might be predicted from the laws of ionization and mass action.

Pfeiffer and Würgler[872] determined the effect of neutral salts on the solubilities of amino acids. They found that the solubilities of most of the acids used were materially increased by the addition of salts, and that the power of increasing solubility seemed to be an additive characteristic of the ions of the salts. Euler[873] suggested that the increase of solubility was due to metathesis between the inorganic salt and the organic acid, as suggested by Lundén[874].

Thorin[875], working with ether as solute, found that while the salting out effect of sodium salts of aliphatic acids was comparable to the effect of salts of inorganic acids, the salts of aromatic acids caused an increase in solubility instead of a decrease.* A confirmation of this result is found in the work of von Euler[876], who reported that sodium salts of inorganic and aliphatic acids decreased the solubility of aniline, nitrobenzene, and ether, but increased the solubilities of sodium salts of aromatic acids. Euler[877] showed that, in general, metallic salts of organic acids which increase surface tension in water decrease the solubility of unionized solutes, while salts like sodium benzoate and aniline nitrate which decrease surface tension cause an increase in solubility of the other solute. Further work in this field, leading to the conclusion that solubility lowering is primarily an ionic effect, was done by Euler and Svanberg[878], by Euler and Rudberg[879], and by Linde[880].

Of the various aspects of the salting out phenomenon, one which is among the most marked, and at the same time the least understood, is the great difference in precipitating effect manifested by different salts. A careful study of this phase of the problem was carried out by Rivett and Rosenblum[881], who determined the solubility at 25° of phthalic acid in pure water and in solutions of varying concentrations of some twenty-five salts. Since phthalic acid is a weak electrolyte, some double decomposition with the salts was to be expected; this was manifested by an initial increase in solubility of the acid over that in pure water as the concentration of salt was increased. The decrease in solubility consequent upon the true salting out effect had overcome the increase caused by double decomposition in those cases in which a maximum was reached and passed. In the instances in which the solubility continually increased with addition of the second solute, this was either an organic liquid (alcohol) in which the acid was more soluble than in water[882], or the salt of an acid comparable in ionic strength with phthalic acid (*e.g.*, potassium acetate); in the latter case the solubility of phthalic acid in a solution 0.547-normal in the salt was nearly twelve times its solubility in pure water.

---

* For the hydrotropic effect of salts of aromatic acids on other solutes, see p. 23.

In cases in which the salting out effect was manifested, it was in general the least electro-positive element which exerted the greatest depressing effect among the chlorides both of the univalent and the divalent metals. If the solubility of phthalic acid in pure water be taken as unity, its solubility in 1-molal solutions of the chlorides of various elements was found to be as follows: Mg 0.46, Ca 0.52, Ba 0.58, Li 0.69, Na 0.74, NH_4 0.86, K 0.88, Rb 0.95, Cs 1.05. For potassium salts the relative solubility of the acid in 0.5-molal solution was as follows: Cl 0.96, Br 0.98, I 1.02, ClO_3 1.03, BrO_3 1.03, NO_3 1.06, IO_3 1.22, SO_4 1.30. The solubility decrease caused by the addition of sodium salts was in all cases markedly greater than that caused by the corresponding potassium salts. In 1-molal hydrochloric acid the relative solubility was 0.64. The temperature coefficient of solubility lowering was determined for potassium chloride and for sodium nitrate over a narrow temperature range; the solubility decrease (value in pure water at the respective temperature = 1.0) was somewhat greater at the higher temperature than at the lower.

For about half the second solutes investigated, a formula was derived by means of which it was possible to calculate the relative solubility lowering with considerable accuracy. These conclusions of Rivett and Rosenblum were in excellent accord with the results obtained by Herz[883], who worked with tartaric acid, using alkali halides as second solutes. When the solution was 2-molal in alkali chloride, the relative solubilities (pure water = 1.0) were Li 0.46, Na 0.64, and K 0.88. For the potassium salts, the salting out power decreased in the order KCl, KBr, KI, but the differences observed were slight. The less extended but more detailed work of Hoffmann and Langbeck[884] was also confirmed in all points common to the two investigations.

Salting out in the laboratory is carried out in a manner similar in general to the industrial methods used in the dyestuff and the soap industries[885]. The solution to be precipitated is cooled and salt free from lumps is added, as a rule until the solution is nearly saturated; the solution is well stirred during this addition to insure complete dissolving of the salt, and to prevent occlusion of lumps of salt by the precipitate. Sometimes better results are obtained by the addition of brine rather than solid salt; this is likely to be the case when the presence of a small quantity of salt causes a marked decrease in solubility of the organic solute, and when the loss in the mother liquor is not great.

The quantity of salt required for maximum precipitation of a given compound can be determined only by experiment. With dyestuffs or other deeply colored compounds, this is readily done by adding salt a little at a time to the solution, and after each addition placing a drop of the mixture on filter paper. The capillarity of the paper will cause the drop to spread; at first almost the entire spot will be colored, but as more salt is added the colored spot will decrease in size, and will be surrounded by a colorless ring. When continued addition of salt produces no further decrease in the size of the colored spot, the precipitation may be considered complete. In some cases it is necessary to approach this point with some caution, to avoid precipitating tar or other impurities which may be present.

Cooke[886] studied the salting out of sodium naphthalene-β-sulfonate at various temperatures with both sodium chloride and sodium sulfate. He found that the solubility of the organic salt was reduced almost to a minimum when the concentration of the precipitant reached 10%; the salting out effect of sodium chloride was distinctly greater under all conditions than that of sodium sulfate. Thorne[887] reported that even small additions of sodium chloride to water decreased the solubility of ether very materially, the value being halved in the presence of 6% of salt. Fühner[288] determined the solubilities of the lower aliphatic alcohols in potassium carbonate solutions of various concentrations, and in pure water. He showed that with a given concentration of salt in the solvent, the solubility of an alcohol was (roughly) four to six times that of the next higher homologous alcohol.*

The question of optimum concentration of precipitant was considered from a different viewpoint by Hochstetter[888]. Ac-

* See also page 50.

cording to the procedure given by Gattermann[889] for the preparation of benzene monosulfonic acid by sulfonation of benzene, the reaction mixture was precipitated by adding it to three or four times its volume of a cold, saturated solution of sodium chloride. This process, according to Hochstetter, gave a product containing on an average 37% of sodium chloride. If instead four volumes of salt solution of sp. gr. 1.151 (about three-fourths saturated) were used, the product contained less than 1% of salt; the yield of pure sulfonic acid in this case was about 5% less than that obtained by the other method.

The decrease in solubility of certain compounds which may be caused by the addition of salt has been utilized in analytical methods which depend on extraction by "shaking-out." For the determination of alcohol in medicinal preparations rich in volatile oils (*e.g.*, tincture of Jamaica Ginger, U.S.P.), the simple method of observing the specific gravity cannot be used, because of the quantity of oil which passes over with the alcoholic distillate. In such cases the Pharmacopœia[890] directs that the distillate be transferred to a separatory funnel, saturated with sodium chloride, and repeatedly extracted with petroleum benzine. Without the addition of salt to decrease the solubility of the oils, the separation by shaking-out would be very incomplete. Beal and Hamilton[891] reported that in the extraction of alkaloids by shaking-out the extraction might be carried out in fewer steps if the aqueous layer was partly saturated with salt.

The fact that different compounds show widely differing susceptibilities to precipitation enables the use of salting out as a method of fractionation. In their work on tannins, Knox and Prescott[892] extracted kola nuts with dilute alcohol and distilled the alcohol from the extract. A part of the caffein kolatannate was precipitated, but the remainder, together with all the kolatannin, remained in solution. When the solution was saturated with sodium chloride, all the caffein kolatannate was precipitated, while the kolatannin remained in solution. In the course of experiments on the purification of an amylase by fractional precipitation with alcohol, Sherman and Tanberg[893] found that often when the addition of alcohol alone was ineffective, a precipitate could be obtained on addition of a little sodium chloride.

It was further found that the use of salt in conjunction with alcohol as a precipitant not only increased the yield, but gave a more effective fractionation.

As various quantitative investigations of salting out have shown, **sodium sulfate** causes much less decrease in the solubility of most organic solutes than does sodium chloride, and for that reason the sulfate has been used as a precipitant only in special cases. The most important type of work in which the use of this salt instead of the chloride is indicated is when the precipitate is to be subjected to sulfonation. In all cases of salting out a certain amount of the inorganic salt is carried down with the precipitate; at times, as Hochstetter has shown, this may amount to a considerable proportion of the total. It is evident that if large quantities of sodium chloride are present in material which is treated with sulfuric acid, the hydrochloric acid liberated by the action of sulfuric acid on the sodium chloride will tend to cause chlorination or other side reactions. While the use of sodium sulfate to precipitate the intermediate compound will probably result in a somewhat smaller yield, the inorganic salt in the precipitate will be entirely inert in the subsequent sulfonation.

An instance in which sodium sulfate manifested greater salting-out powers than sodium chloride was reported by Gomberg[894]. An aqueous solution of chlorohydrin, saturated with sodium chloride, contained 16–17% of chlorohydrin; the oil which separated was about 30% water and 70% chlorohydrin, and each hundred cubic centimeters contained 7.2 g. of salt. At room temperature, addition of sodium sulfate had very little effect, but if the chlorohydrin solution was saturated with the sulfate at slightly higher temperatures (32–3°) the aqueous layer retained only about 7% of chlorohydrin. In this case the oil contained about the same proportion of water as before, but only 0.68 g. per 100 cc. of sodium sulfate. The following procedure was found of advantage when working on a laboratory scale: after all the chlorohydrin had separated from the solution saturated at 32° with sodium sulfate, the mixture was allowed to cool without agitation. When a crystal of the salt was dropped into the cooled solution, crystallization in the supersaturated aqueous solution ensued at the point of juncture of the two liquids; so dense was the mass of crystals that the oil could be decanted without contamination from the lower layer.

Sodium acetate has also been used as a precipitant for salting out. Baeyer[895] prepared the ethyl ester of amidophthalic acid by reduction of the corresponding nitro compound with zinc dust. After filtration the solution was almost neutralized with soda, and sodium acetate was added; the ester separated in oily drops which soon crystallized. A similar procedure was also used by Baeyer[896] for preparing amidoindigo. Weinberg[897] reported that if sodium acetate was added to an aqueous solution of the hydrochloride of diamino oxyphenyltolyl sulfonic acid, a copious precipitate of the free acid was formed.

The following method was developed by Lubs[898] for the purification of certain technical azo dyestuffs, which generally contain much inert matter, both organic and inorganic. Fifty grams of the dye were dissolved in 100 cc. of distilled water and filtered; to the boiling solution enough solid sodium acetate was added (about 350 g.) to precipitate the dye as completely as possible. The dye was filtered and pressed free from mother liquor; any sodium acetate present was removed by boiling with successive portions of 95% alcohol (about 250 cc. each). This method of purification is of course applicable only to dyes which can be precipitated with sodium acetate, and which are relatively insoluble in 95% alcohol, but with the dyes used by Lubs (Brilliant Congo R, Azorubin, and Congo Red) excellent results were obtained.

Ammonium chloride was used by Hantzsch and Robison[899] to decrease the solubility of murexide in aqueous solution, and thereby to bring about true crystallization. A saturated solution of the impure material, free from suspended matter, was treated with ammonium chloride, and crystallization was induced by scratching the glass; conductivity determinations showed that the resulting crystals were perfectly pure. Heidelberger and Jacobs[900] prepared hydroxyphenyl-azo-hydrocupreine by treating the benzoyl derivative in alcoholic solution with strong sodium hydroxide. When the hydrolysis was complete, water was added, and the dyestuff was precipitated by addition of saturated ammonium chloride solution.

Kühne and Chittenden[901] found that pure peptones, free from albumens, might be obtained by addition of an excess of solid **ammonium sulfate** to the solution of the two compounds, slightly acidified with acetic acid. The excess salt and precipitated albumens were filtered off, and pure peptone was obtained as the barium salt from the clear liquid. This procedure was subsequently modified[902] by precipitating first in acid solution, as before, and removing the last traces of albumen by a further treatment in neutral or ammoniacal solution. Before precipitating the peptonate, the greater part of the ammonium sulfate was removed by concentrating the solution. Reichert[903] reported that in the customary method for preparing crystals of oxyhemoglobin from blood — by laking the blood with ether and subjecting it to cold — crystallization sometimes took place only after many hours. If a few percent of **ammonium oxalate** were added to the blood, before or after laking, crystallization invariably began immediately, even at room temperature; this procedure was particularly advantageous for work under the microscope.

The use of **sodium** or **potassium hydroxide** for salting out has occasionally been of value. Otto[904] observed that the salts of sulfinic acids might be precipitated from their aqueous solutions by the addition of strong caustic, and Pinnow and Pistor[905] removed tar from a solution of *p*-formylamino dimethyl aniline by saturating the solution with salt and adding caustic soda; the solution was filtered and the free base obtained by extraction with ether. Wienhaus[906] prepared tetrahydrofurfuralcohol by catalytic reduction of furfuralcohol, but was unable to separate the reduction product by shaking-out with ether because of hydrate formation; complete separation was attained, however, by saturating the aqueous solution with potassium hydroxide. As was mentioned on page 50, Lassar-Cohn[287] made practical use in extractions of the fact that alcohol is insoluble in concentrated aqueous solutions of **potassium carbonate.**

An instance of the use of the common-ion effect to bring about the separation of an organic compound was reported by Kober[907]. Arsphenamine dihydrochloride was by the common-ion effect insoluble in an excess of hydrochloric acid. The base was dissolved in sodium hydroxide, a slight excess of hydrochloric acid was added, and the solution was poured into 1–1 hydrochloric acid. A white precipitate was formed, but this soon changed to a black gum, owing to coalescence of the particles. This undesirable after-effect was prevented by precipitating at a low temperature (0°) with vigorous stirring, and by the use of large volumes of solution; the reaction mixture from 85 g. of crude nitrooxyphenyl arsonic acid was diluted to 1700 cc. and slowly poured into 3250 cc. of acid.

A novel method for the precipitation of solutes in alcohol, ether, or chloroform was proposed by Weitenkampf[908]. The solution was cooled with ice and salt, and saturated with carbon dioxide under 3–4 atmospheres pressure. In the purification of raw spirit, the oils were thrown out in this way, and the mixture, still under pressure, was filtered through charcoal.

BIBLIOGRAPHY

ABBREVIATIONS

Am. Chemist	American Chemist
Am. Chem. J.	American Chemical Journal
Am. J. Pharm.	American Journal of Pharmacy
Am. J. Physiol.	The American Journal of Physiology
Analyst	The Analyst
Ann.	Annalen der Chemie (Liebig)
Ann. chim.	Annales de chimie
Ann. chim. anal. chim. appl.	Annales de chimie analytique et de chimie appliquée
Ann. chim. phys.	Annales de chimie et de physique
Ann. Physik Chem.	Annalen der Physik und Chemie (Poggendorff-Wiedemann)
Arch. exptl. Path. Pharmakol.	Archiv für experimentelle Pathologie und Pharmakologie
Arch. Pharm.	Archiv der Pharmazie
Atti VI Cong. internaz. chim. applicata	Atti del VI Congresso internazionale di chimica applicata
Ber.	Berichte der deutschen chemischen Gesellschaft
Biochem. J.	The Biochemical Journal
Brennstoff-Chem.	Brennstoff-Chemie
Brit.	British Patent
Brit. Assoc. Advancement Sci., Repts.	British Association for the Advancement of Science, Reports
Bull. acad. sci. St. Petersburg.	Bulletin de l'académie des sciences, St. Petersburg
Bull. assoc. chim. sucr. dist.	Bulletin de l'association des chimistes de sucrerie et de distillerie
Bull. soc. chim.	Bulletin de la société chimique de France
Bull. soc. chim. Belg.	Bulletin de la société chimique de Belgique
Bull. soc. chim. biol.	Bulletin de la société de chimie biologique
Bull. soc. encour. ind. nat.	Bulletin de la société d'encouragement pour l'industrie nationale
Bur. Mines Tech. Paper	Bureau of Mines Technical Paper
Bur. Standards Bull.	Bureau of Standards Bulletin
Bur. Standards Circ.	Bureau of Standards Circular
C. A.	Chemical Abstracts (annual volumes since 1907)
Can.	Canadian Patent
Can. Chem. Met.	Canadian Chemistry and Metallurgy
Caoutchouc et gutta-percha	Le caoutchouc et la gutta-percha
Chem. Met. Eng.	Chemical and Metallurgical Engineering

Chem. News	The Chemical News and Journal of Industrial Science
Chem. Umschau	Chemische Umschau auf dem Gebiete der Fette, Oele, Wachse und Harze
Chem. Ztg.	Chemiker Zeitung
Chimie et industrie	Chimie et industrie
Compt. rend.	Comptes rendus hebdomadaires des séances de l'académie des sciences
Fr.	French Patent
Frd.	P. Friedlaender: "Fortschritte der Teerfarbenfabrikation" Vol. I 1877–1887 II 1887–1890 III 1890–1894 IV 1894–1897 V 1897–1900 VI 1900–1902 VII 1902–1904 VIII 1905–1907 IX 1908–1910 X 1910–1912 XI 1912–1914 XII 1914–1916 XIII 1916–1921
Gazz. chim. ital	Gazzetta chimica italiana
Ger.	German Patent
Giorn. chim. ind. applicata	Giornale di chimica industriale ed applicata
Helvetica Chim. Acta	Helvetica Chimica Acta
Ind. Eng. Chem.	Industrial and Engineering Chemistry
India Rubber J.	India Rubber Journal
India Rubber World	India Rubber World
Jahresber.	Jahresbericht über die Fortschritte der Chemie
J. Am. Chem. Soc.	Journal of the American Chemical Society
J. Am. Pharm. Assoc.	Journal of the American Pharmaceutical Association
J. Anal. Chem.	Journal of Analytical Chemistry
J. Biol. Chem.	The Journal of Biological Chemistry
J. Chem. Soc.	Journal of the Chemical Society (London), Transactions
J. Chem. Soc. Abstr.	Journal of the Chemical Society (London), Abstracts
J. chim. phys.	Journal de chimie physique
J. Ind. Eng. Chem.	The Journal of Industrial and Engineering Chemistry
J. pharm. chim.	Journal de pharmacie et de chimie
J. Phys. Chem.	The Journal of Physical Chemistry
J. Physiol.	The Journal of Physiology
J. prakt. Chem.	Journal für praktische Chemie
J. Russ. Phys.-Chem. Soc.	Journal of the Russian Physical-Chemical Society

J. Soc. Chem. Ind.	Journal of the Society of Chemical Industry
J. Soc. Dyers Colourists	Journal of the Society of Dyers and Colourists
J. Wash. Acad. Sci.	Journal of the Washington Academy of Sciences
Kolloid-Z.	Kolloid-Zeitschrift
Kunststoffe	Kunststoffe
Mem. Coll. Sci. Eng. Kyoto Imp. Univ.	Memoirs of the College of Science and Engineering, Kyoto Imperial University
Met. Chem. Eng.	Metallurgical and Chemical Engineering
Midland Druggist	The Midland Druggist and Pharmaceutical Review
Monatsh.	Monatshefte für Chemie
Oliën, Vetten en Oliezaden	Oliën, Vetten en Oliezaden
Paper Trade J.	Paper Trade Journal
Pharm. J.	The Pharmaceutical Journal and Pharmacist
Phil. Mag.	The London, Edinburgh and Dublin Philosophical Magazine and Journal of Science
Phil. Trans.	Philosophical Transactions of the Royal Society of London
Physik. Z.	Physikalische Zeitschrift
Proc. Acad. Sci. Amsterdam	Proceedings of the Royal Academy of Sciences of Amsterdam
Proc. Chem. Soc.	Proceedings of the Chemical Society (London)
Proc. Iowa Acad. Sci.	Proceedings of the Iowa Academy of Science
Proc. Roy. Soc. (London)	Proceedings of the Royal Society (London)
Proc. Trans. Nova Scotian Inst. Sci.	The Proceedings and Transactions of the Nova Scotian Institute of Science
Rec. trav. chim.	Recueil des travaux chimiques des Pays-Bas
Science	Science
Trans. Faraday Soc.	Transactions of the Faraday Society
Trans. Roy. Soc. S. Africa	Transactions of the Royal Society of South Africa
Trans. Wisconsin Acad. Sci.	Transactions of the Wisconsin Academy of Sciences, Arts and Letters
U. S.	United States Patent
U. S. P.	United States Pharmacopœia
Win.	Adolf Winther: "Patente der Organischen Chemie" (1908–10)
Z. anal. Chem.	Zeitschrift für analytische Chemie
Z. angew. Chem.	Zeitschrift für angewandte Chemie
Z. anorg. Chem.	Zeitschrift für anorganische Chemie
Z. Biol.	Zeitschrift für Biologie
Z. Chem.	Zeitschrift für Chemie
Z. Chem. Ind. Kolloide	Zeitschrift für Chemie und Industrie der Kolloide
Z. Elektrochem.	Zeitschrift für Elektrochemie
Zentr.	Chemisches Zentralblatt
Z. Farben Textil-Ind.	Zeitschrift für Farben und Textil-Industrie
Z. komprimierte flüssige Gase Pressluft-Ind.	Zeitschrift für komprimierte und flüssige Gase sowie für die Pressluft-Industrie

Z. Nahr. Genussm.	Zeitschrift für Untersuchen der Nahrungs- und Genussmittel
Z. physik. Chem.	Zeitschrift für physikalische Chemie
Z. physik. chem. Unterricht	Zeitschrift für den physikalischen und chemischen Unterricht
Z. physiol. Chem.	Zeitschrift für physiologische Chemie
Z. wiss. Phot.	Zeitschrift für wissenschaftliche Photographie, Photophysik, und Photochemie

REFERENCES

1. V. R. Kokatnur. *J. Am. Chem. Soc.* **41** (1919), 120.
2. G. W. Jones and V. C. Allison. *J. Ind. Eng. Chem.* **11** (1919), 639; *Bur. Mines Tech. Paper* **255** (1921).
3. K. Reimer and Ferd. Tiemann. Ber. **9** (1876), 423, 1268.
4. M. C. Traub. Ger. 80,195 (1895); *Frd.* **IV**, 1287; *Win.* **I**, 484.
5. C. C. Loomis. U. S. 1,384,909 (1921) [*C. A.* **15**, 3850].
6. R. von Walther and R. Hübner. *J. prakt. Chem.* [2] **93** (1916), 120 [*C. A.* **11**, 1629].
7. P. Walden and M. Centnerszwer. *Z. physik. Chem.* **39** (1902), 561 [*Zentr.* **1902 I**, 556, 1039].
8. Felix Jacobsohn. *Z. komprimierte flüssige Gase Pressluft-Ind.* **10** (1907), 37, 53 [*C. A.* **1**, 1666].
9. P. Walden. *Z. physik. Chem.* 1903–08.
10. A. A. Noyes and M. S. Sherrill. "General Principles of Chemistry" (Macmillan, New York, 1920), p. 23.
11. W. H. Dehn. *J. Am. Chem. Soc.* **39** (1917), 1402.
12. S. L. Bigelow. "Theoretical and Physical Chemistry" (Century, New York, 1914), p. 335.
13. Iwan Ostromysslensky. *J. prakt. Chem.* [2] **76** (1908), 264 [*C. A.* **2**, 741].
14. Thomas Carnelly and Andrew Thomson. *J. Chem. Soc.* **53** (1888), 791.
15. J. H. Hildebrand. "Solubility" (Chemical Catalog Co., New York, 1924), p. 38.
16. A. S. McDaniel. *J. Phys. Chem.* **15** (1911), 587 [*C. A.* **5**, 3529].
17. Gerhard Just. *Z. physik. Chem.* **37** (1901), 342 [*Zentr.* **1901 II**, 81].
18. J. H. Walton and C. R. Wise. *J. Am. Chem. Soc.* **44** (1922), 103.
19. Harold Deane and W. E. Edmonton. *Pharm. J.* **106** (1921), 469, 499 [*C. A.* **16**, 462].
20. E. B. Hunn. *J. Am. Chem. Soc.* **45** (1923), 1026.
21. M. T. Bogert and W. F. Hand. *J. Am. Chem. Soc.* **27** (1905), 1480.
22. H. G. Rule. *J. Chem. Soc.* **113** (1918), 12 [*C. A.* **12**, 677].
23. B. Landau. *Chem. Ztg.* **34** (1910), 1032 [*C. A.* **5**, 3747].
24. H. de Mosenthal. *J. Soc. Chem. Ind.* **23** (1904), 295.
25. Mehren. *Kunststoffe* **12** (1922) 99, 105 [*C. A.* **16**, 3548].
26. Otto Dimroth and Curt Bamberger. *Ann.* **438** (1924), 58, 67 [*C. A.* **18**, 2504].
27. R. J. Manning. *J. Am. Chem. Soc.* **32** (1910), 1314.
28. A. C. Oudemans. *Ann.* **166** (1873), 74 [*J. Chem. Soc. Abstr.* **26** (1873) i, 461; *Zentr.* **1873**, 241].

29. G. Gallotti and G. Giampalmo. *Z. chem. ind. Kolloide* **3** (1908), 118 [*C. A.* **3**, 856].
30. R. H. Chittenden and T. B. Osborne. *Am. Chem. J.* **14** (1892), 32 [*Zentr.* **1892 I**, 559].
31. J. W. Marden and M. V. Dover. *J. Am. Chem. Soc.* **39** (1917), 3.
32. Ger. 85,231 (1896); *Frd.* **IV**, 376; *Win.* **II**, 356.
33. Ger. 85,232 (1896); *Frd.* **IV**, 377; *Win.* **II**, 369.
34. Rudolf Schenck and G. Römer. *Ber.* **57**B (1924), 1345 [*C. A.* **18**, 3565].
35. Walther Löb. *Ber.* **30** (1897), 1573.
36. L. P. Kyrides. U. S. 1,466,535 (1923) [*C. A.* **17**, 3881].
37. R. R. Renshaw and G. E. Holm. *J. Am. Chem. Soc.* **42** (1920), 1470.
38. M. Hayduck. *Ann.* **167** (1873), 180 [*Zentr.* **1873**, 533].
39. Georg Zetter. *Ber.* **11** (1878), 169.
40. S. Palkin. *Ind. Eng. Chem.* **15** (1923), 379.
41. W. G. Bateman and D. B. Conrad. *J. Am. Chem. Soc.* **37** (1915), 2533.
42. Leroy McMaster. *J. Am. Chem. Soc.* **36** (1914), 1923.
43. Leroy McMaster and A. C. Magill. *J. Am. Chem. Soc.* **38** (1916), 1788.
44. J. Guareschi. *Gazz. chim. ital.* **4** (1874), 466 [*J. Chem. Soc. Abstr.* **28** (1875) i, 569].
45. B. L. West. *J. Am. Chem. Soc.* **42** (1920), 1659.
46. L. H. Friedburg and J. A. Mandel. *J. Am. Chem. Soc.* **12** (1890), 57.
47. S. J. C. Olivier. *Rec. trav. chim.* **36** (1916), 117 [*C. A.* **11**, 2894].
48. N. Menschutkin. *Z. physik. Chem.* **6** (1890), 41 [*Zentr.* **1890 II**, 573].
49. T. S. Patterson and H. H. Montgomerie. *J. Chem. Soc.* **101** (1912), 26 [*C. A.* **6**, 958].
50. J. A. Hawkins. *J. Chem. Soc.* **121** (1922), 1170 [*C. A.* **16**, 3247].
51. P. W. Carleton. *J. Am. Chem. Soc.* **38** (1916), 1132.
52. Francis Arnall. *J. Chem. Soc.* **125** (1924), 811 [*C. A.* **18**, 2142].
53. N. Menschutkin. *Zentr.* **1890 II**, 573; *Ber.* **30** (1897), 2775, 2966; *Zentr.* **1898 I**, 700; *Zentr.* **1900 I**, 1071; *Z. physik. Chem.* **34** (1900) 157 [*Zentr.* **1900 II**, 416].
54. G. Carrara. *Zentr.* **1894 I**, 763.
55. A. von Hemptinne and A. Bekaert. *Z. physik. Chem.* **28** (1899), 225 [*Zentr.* **1899 I**, 814].
56. W. Sagrebin. *Zentr.* **1899 I**, 1059.
57. J. W. Brühl. *Ber.* **32** (1899), 2326; *Z. physik. Chem.* **30** (1899), 1 [*Zentr.* **1899 II**, 956].
58. O. Dimroth. *Ann.* **325** (1904), 1; **338** (1905), 143; **377** (1910), 127 [*Zentr.* **1904 II**, 1228; **1905 I**, 1164; **1911 I**, 154].
59. C. Tubandt. *Ann.* **354** (1907), 259 [*Zentr.* **1907 II**, 1167].
60. J. B. Cohen. "Organic Chemistry for Advanced Students" (Longmans, Green, New York, 1918) **I**, p. 326.
61. T. F. Brown. *Pharm. J.* [3] **4** (1874), 729 [*J. Chem. Soc. Abstr.* **27** (1874), 723].
62. Ed. Schar. *Arch. Pharm.* **233** (1895), 5 [*Zentr.* **1895 I**, 852].
63. O. Wallach. *Ann.* **262** (1891), 340 [*Zentr.* **1891 I**, 792].
64. F. L. Dunlap. *J. Am. Chem. Soc.* **24** (1902), 761.
65. F. J. Moore. *J. Am. Chem. Soc.* **28** (1906), 1188.
66. W. D. Bancroft. *J. Phys. Chem.* **1** (1896), 137 [*Zentr.* **1897 I**, 152].
67. R. W. Moore. *J. Am. Chem. Soc.* **41** (1919), 1060.

68. P. Jannasch and A. Bartels. *Ber.* **31** (1898), 1716.
69. G. A. Burrell *et al.* *J. Am. Chem. Soc.* 1914–15; *J. Ind. Eng. Chem.* 1915.
70. J. H. Hildebrand. Reference 15, p. 160.
71. J. H. Hildebrand. Reference 15, various sections; also bibliography of work by Hildebrand and his co-workers.
72. F. S. Mortimer. *J. Am. Chem. Soc.* **44** (1922), 1416; **45** (1923), 633.
73. Edw. Haworth and W. H. Perkin, Jr. *J. Chem. Soc.* **69** (1896), 175.
74. W. R. Orndorff and E. F. Hitch. *J. Am. Chem. Soc.* **36** (1914), 691.
75. Heinrich Wieland and Wilhelm Rheinheimer. *Ann.* **423** (1921), 17 [*C. A.* **15**, 2634].
76. S. R. Benedict. *J. Biol. Chem.* **54** (1922), 239 [*C. A.* **17**, 116].
77. Fritz Ullman and Géza Nádai. *Ber.* **41** (1908), 1871 [*C. A.* **2**, 2697].
78. J. M. Clark. *J. Ind. Eng. Chem.* **11** (1919), 204.
79. C. L. Jackson and W. S. Robinson. *Am. Chem. J.* **11** (1889), 551 [*J. Chem. Soc. Abstr.* **58** (1890), 377].
80. Wilhelm Wislicenus and Rudolf Erbe. *Ann.* **421** (1920), 121 [*C. A.* **15**, 503].
81. J. F. Norris. *J. Am. Chem. Soc.* **38** (1916), 702.
82. M. Schöpff. *Ber.* **25** (1892), 1981.
83. P. Latschinoff. *Ber.* **20** (1887), 1046.
84. Lassar-Cohn. *Ber.* **26** (1893), 147.
85. R. H. McKee and E. J. Berkheiser. *Am. Chem. J.* **40** (1908), 303 [*C. A.* **2**, 3026].
86. S. Posternak. *Helvetica Chim. Acta* **4** (1921), 156 [*C. A.* **15**, 1891].
87. Julius Schmidlin and Paul Massini. *Ber.* **42** (1909), 2398 [*C. A.* **3**, 2558].
88. Eduard Büchner and H. Witter. *Ber.* **25** (1892), 1159.
89. Arno Behr. *J. Am. Chem. Soc.* **4** (1882), 11.
90. G. Wyrouboff. *Ann. chim. phys.* [7] **1** (1894), 44 [*Zentr.* **1894 I**, 260].
91. Lassar-Cohn. "Arbeitsmethoden" Ed. IV, Vol. I (Voss, Hamburg, 1906), p. 157.
92. C. A. Lobry de Bruyn. *Z. physik. Chem.* **10** (1892), 788 [*Zentr.* **1893 I**, 599].
93. O. Hesse. *Ann.* **225** (1884), 247 [*Zentr.* **1884**, 936].
94. J. E. Marsh. *J. Chem. Soc.* **105** (1914), 2368 [*C. A.* **9**, 171].
95. Calloud and C. Brunner. *Ann.* **31** (1839), 195.
96. Emil Fischer and Eduard Schmidmer. *Ann.* **272** (1893), 165 [*J. Chem. Soc. Abstr.* **64** (1893) ii, 109].
97. H. Kolbe and E. Lautemann. *Ann.* **119** (1861), 139.
98. F. Herrmann. *Ber.* **19** (1886), 2235.
99. A. Hantzsch and F. Herrmann. *Ber.* **20** (1887), 2810.
100. H. Hlasiwetz and L. Barth. *Ann.* **134** (1865), 278 [*Zentr.* **1865**, 577].
101. Rudolf Cohn. *Z. physiol. Chem.* **17** (1892), 306 [*Zentr.* **1892 II**, 836].
102. W. Herz. *Ber.* **31** (1898), 2669.
103. C. W. Clifford. *J. Ind. Eng. Chem.* **13** (1921), 632.
104. John Wade and Horace Finnemore. *J. Chem. Soc.* **95** (1909), 1849 [*C. A.* **4**, 702].
105. G. S. Forbes and A. S. Coolidge. *J. Am. Chem. Soc.* **41** (1919), 154.
106. E. Groschuff. *Z. Elektrochem.* **17** (1911), 348 [*C. A.* **5**, 2550].
107. R. E. Wilson. *J. Am. Chem. Soc.* **43** (1921), 715.
108. A. A. Noyes and L. R. Westbrook. *J. Am. Chem. Soc.* **43** (1921), 729.
109. H. Führer. *Ber.* **57**B (1924), 514 [*C. A.* **18**, 2493].

110. Newton Harvey. *J. Am. Chem. Soc.* **37** (1915), 398.
111. Rasik Lal Datta and S. Das Gupto. *J. Am. Chem. Soc.* **37** (1915), 581.
112. Latham Clarke and W. N. Jones. *J. Am. Chem. Soc.* **34** (1912), 172.
113. Franz Fischer and Albert Jaeger. *Brennstoff-Chem.* **4** (1923), 225, 241, 259, 261 [*C. A.* **18**, 320, 459].
114. H. G. Deming. *J. Am. Chem. Soc.* **33** (1911), 1515.
115. R. Palm. *Z. anal. Chem.* **22** (1883), 323 [*J. Chem. Soc. Abstr.* **46** (1884), 83; *Zentr.* **1883**, 615].
116. H. L. Wollenberg and C. A. Bigelow. U. S. 1,297,524 (1919) [*C. A.* **13**, 1594].
117. E. Schunck and H. Roemer. *Ber.* **10** (1877), 175, 551.
118. Carl Neuberg. *C. A.* **11**, 256, 1437; *Zentr.* **1916 II**, 970, 971.
119. O. N. Witt. *Ber.* **48** (1915), 747 [*C. A.* **9**, 2094].
120. Friedrich Nottbrack. *Chem. Ztg.* **32** (1908), 100 [*Zentr.* **1908 I**, 778].
121. G. Link. Ger. 35,168 (1885); *Frd.* **I**, 11; *Win.* **I**, 790.
122. Robert Otto. *Ber.* **27** (1894), 2131.
123. R. Heuter. *Kunststoffe* **13** (1923), 13 [*C. A.* **18**, 2568].
124. Paul Dietze. U. S. 1,405,902 (1922) [*C. A.* **16**, 133].
125. G. A. Raupenstrauch. *Arch. Pharm.* **229** (1891), 201 [*Zentr.* **1891 I**, 135].
126. F. von Heyden. Ger. 57,842 (1890); *Win.* **I**, 191.
127. Eduard Ritsert. Ger. 147,790 (1903), 149,345 (1904); *Frd.* **VII**, 639; *Win.* **I**, 570.
128. Ger. 148,943 (1904); *Frd.* **VII**, 275; *Win.* **II**, 502
Ger. 160,783 (1905); *Frd.* **VIII**, 423; *Win.* **II**, 502.
Ger. 172,465 (1906); *Frd.* **VIII**, 838.
129. O. Maass and W. H. Hatcher. *J. Am. Chem. Soc.* **42** (1920), 2548.
130. Max Bamberger and Josef Nussbaum. *Monatsh.* **40** (1919), 411 [*C. A.* **14**, 1810].
131. O. Maass and W. H. Hatcher. *J. Am. Chem. Soc.* **44** (1922), 2473.
132. J. H. Walton and H. A. Lewis. *J. Am. Chem. Soc.* **38** (1916), 633.
133. H. T. Calvert. *Z. physik. Chem.* **38** (1901), 521 [*J. Chem. Soc. Abstr.* **82** (1902) ii, 10].
134. J. C. Cain and J. F. Thorpe. "Synthetic Dyestuffs and Intermediate Products" (Griffin, London, 1917), p. 55.
135. G. Schultz. "Farbstofftabellen" (Wiedmann, Berlin, 1914).
136. A. G. Green. "A Systematic Survey of the Organic Colouring Matters" (Macmillan, London, 1908).
137. J. C. Cain and J. F. Thorpe. Reference 134, p. 336.
138. James Moir. *Trans. Roy. Soc. So. Africa* **11** (1924), 91 [*C. A.* **18**, 1232].
139. R. Weissgerber. *Ber.* **47** (1914), 3176 [*C. A.* **9**, 801]; Ger. 285,666 (1915) [*Frd.* **XII**, 151].
140. J. E. G. Harris and W. J. Pope. *J. Chem. Soc.* **121** (1922), 1029 [*C. A.* **16**, 2865].
141. Leone Oyster and Homer Adkins. *J. Am. Chem. Soc.* **43** (1921), 208.
142. Jos. Knox and H. R. Will. *J. Chem. Soc.* **115** (1919), 850 [*C. A.* **13**, 2858].
143. Viktor Vesely and Emil Votocek. Ger. 164,508 (1904); *Frd.* **VIII**, 227; *Win.* **I**, 943.
144. Thos. Ewan and J. G. Young. *J. Soc. Chem. Ind.* **40** (1921), 110T [*C. A.* **15**, 3272].
145. J. D. Riedel. Ger. 52,982 (1889); *Frd.* **II**, 551; *Win.* **I**, 32.

146. A. W. Dox and Lester Yoder. *J. Am. Chem. Soc.* **43** (1921), 1368.
147. Hermann Lonnies. *Ber.* **13** (1880), 704.
148. K. Heine. *Ber.* **5** (1872), 491.
149. Adolf Baeyer. *Ann.* **127** (1863), 26 [*Zentr.* **1864**, 97].
150. Vezio Vender. Fr. 405,812 (1910) [*C. A.* **5**, 1662].
151. William Kirby. U. S. 1,348,722 (1920) [*C. A.* **14**, 2936].
152. C. L. Jackson and W. R. Lamar. *Am. Chem. J.* **18** (1896), 681 [*Zentr.* **1896 II**, 969].
153. John Stenhouse and C. E. Groves. *Ann.* **188** (1877), 354; *J. Chem. Soc.* **31** (1877), 546 [*Zentr.* **1877**, 659].
154. Fr. Fichter and Wolfgang Jaeck. *Helvetica Chim. Acta* **4** (1921), 1001 [*C. A.* **16**, 710].
155. Fr. Fichter and Gustav Grisard. *Helvetica Chim. Acta* **4** (1921), 928 [*C. A.* **16**, 713].
156. M. Battegay and G. Hugel. *Bull. soc. chim.* [4] **27** (1920), 557 [*C. A.* **15**, 1498].
157. O. L. Brady and P. N. Williams. *J. Chem. Soc.* **117** (1920), 1139 [*C. A.* **15**, 372].
158. W. Will. *Ber.* **28** (1895), 369.
159. T. B. Johnson and A. J. Hill. *J. Am. Chem. Soc.*, **38** (1916), 1394.
160. F. W. Schlieper. *Ber.* **25** (1892), 552.
161. A. V. Blom. *Helvetica Chim. Acta* **4** (1921), 302 [*C. A.* **15**, 3996].
162. M. T. Bogert and M. R. Mandelbaum. *J. Am. Chem. Soc.* **45** (1923), 3052.
163. E. C. Sherrard and A. W. Froehlke. *J. Am. Chem. Soc.* **45** (1923), 1730.
164. Conrad Laar. *Ber.* **14** (1881), 1933.
165. H. Wales. *J. Ind. Eng. Chem.* **14** (1922), 317.
166. Emil Fischer. *Ber.* **39** (1906), 4144.
167. W. Lenz. *Ber.* **12** (1879), 581.
168. Alexander Lowy and R. F. Dunbrook. *J. Am. Chem. Soc.* **44** (1922), 616.
169. L. A. Bigelow. *J. Am. Chem. Soc.* **44** (1922), 2010.
170. A. J. Quick. *J. Am. Chem. Soc.* **42** (1920), 1038.
171. M. T. Bogert and M. R. Mandelbaum. *J. Am. Chem. Soc.* **45** (1923), 3051.
172. Alfred Stock. *Ber.* **47** (1914), 154 [*C. A.* **8**, 1248]; **50** (1917), 989 [*C. A.* **12**, 547].
173. E. C. Franklin and C. A. Kraus. *Am. Chem. J.* **21** (1898), 8 [*Zentr.* **1899 I**, 515].
174. E. C. Franklin and C. A. Kraus. *Am. Chem. J.* **20** (1898), 820 [*Zentr.* **1899 I**, 330]; see also *ibid.*, **23** (1900), 301 [*Zentr.* **1900 I**, 1188].
175. G. Gore. *Proc. Roy. Soc.* (*London*) **20** (1872), 441; **21** (1873), 140 [see *Zentr.* **1872**, 707].
176. Edward Bartow and D. F. McFarland. *J. Am. Chem. Soc.* **24** (1902), R303.
177. E. C. Franklin. *J. Am. Chem. Soc.* **44** (1922), 490.
178. E. C. Franklin and O. F. Stafford. *Am. Chem. J.* **28** (1902), 83 [*Zentr.* **1902 II**, 787].
179. C. A. Kraus and G. F. White. *J. Am. Chem. Soc.* **45** (1923), 768.
180. G. F. White. *J. Am. Chem. Soc.* **45** (1923), 779.
181. G. F. White. *J. Am. Chem. Soc.* **45** (1923), 783.
182. E. Chablay. *Ann. chim.* [9] **1** (1914), 510 [*C. A.* **8**, 3422].
183. F. B. Dains *et al.* *J. Am. Chem. Soc.* **40** (1918), 936.
184. C. W. Clifford. *J. Am. Chem. Soc.* **41** (1919), 1051.

185. F. B. Dains and R. Q. Brewster. *J. Am. Chem. Soc.* **42** (1920), 1573.
186. C. A. Kraus and W. N. Greer. *J. Am. Chem. Soc.* **44** (1922), 2630.
187. Thomas Wilton. Ger. 113,291 (1900); *Frd.* **VI**, 47; *Win.* **I**, 942.
188. J. C. Clancy. U. S. 1,423,710–1 (1922) [*C. A.* **16**, 3202].
189. J. C. Clancy. U. S. 1,439,293 (1922) [*C. A.* **17**, 879; *Chem. Met. Eng.* **28** (1923), 128].
190. P. Walden. *Ber.* **32** (1899), 2862; see also ref. 7.
191. A. R. Grob and C. C. Adams. U. S. 1,422,564 (1922) [*C. A.* **16**, 3094; *Chem. Met. Eng.* **27** (1922), 656].
192. Gerhard Schmitt. *C. A.* **16**, 3745; **17**, 3390; *Zentr.* **1923 II**, 300.
193. H. Plauson. Brit. 156,123 (1920) [*C. A.* **15**, 1804]; Can. 220,515 (1922) [*C. A.* **16**, 2944]; U. S. 1,436,289 (1922) [*C. A.* **17**, 627].
194. R. J. Moore *et al.* *Met. Chem. Eng.* **18** (1918), 398 [*C. A.* **12**, 1923].
195. V. K. Krieble and W. F. Seyer. *J. Am. Chem. Soc.* **43** (1921), 1343.
196. L. Edeleanu. *Z. angew. Chem.* **36** (1923), 573 [*C. A.* **18**, 750].
197. R. H. McKee and D. E. Cable. *Paper Trade J.* **77** #16 (Oct. 18, 1923), 101 [*C. A.* **18**, 466].
198. R. H. McKee and A. A. Holmes. U. S. 1,360,658 (1920) [*C. A.* **15**, 597].
199. Ger. 68,474 (1893); *Frd.* **III**, 194; *Win.* **I**, 942.
200. E. H. Archibald. *J. Am. Chem. Soc.* **34** (1912), 584; *J. chim. phys.* **11** (1913), 741 [*C. A.* **8**, 1371].
201. E. H. Archibald. *J. Am. Chem. Soc.* **29** (1907), 682.
202. E. H. Archibald. *J. Am. Chem. Soc.* **29** (1907), 1420.
203. O. Maass and D. McIntosh. *J. Am. Chem. Soc.* **33** (1911), 70.
204. B. D. Steele *et al.* *Phil. Trans.* A**205** (1905), 121 [see *Zentr.* **1906 I**, 1597].
205. E. H. Archibald and Douglas McIntosh. *J. Chem. Soc.* **85** (1904), 924.
206. O. Maass and D. McIntosh. *J. Am. Chem. Soc.* **34** (1912), 1273.
207. Douglas McIntosh. *J. Am. Chem. Soc.* **28** (1906), 588.
208. E. H. Büchner. *Z. physik. Chem.* **54** (1906), 665 [*Zentr.* **1906 I**, 1239].
209. G. Gore. *Phil. Trans.* **151** (1861), 86.
210. U. Antony and G. Magri. *Gazz. chim. ital.* **35** (1905), 219 [*Zentr.* **1905 I**, 1691].
211. J. W. Walker *et al.* *J. Chem. Soc.* **85** (1904), 1098.
212. G. N. Quam. *J. Am. Chem. Soc.* **47** (1925), 107.
213. Victor Lenher. *J. Am. Chem. Soc.* **43** (1921), 29; U. S. 1,385,081 (1921) [*C. A.* **15**, 3728]; see also J. *Am. Chem. Soc.* **44** (1922), 1664.
214. Victor Lenher. *J. Am. Chem. Soc.* **44** (1922), 1668.
215. Felix Jacobsohn. *Z. komprimierte flüssige Gase Pressluft-Ind.* **10** (1907), 60 [*C. A.* **1**, 1666].
216. St. von Laszczynski. *Ber.* **27** (1894), 2285.
217. A. P. N. Franchimont. *Rec. trav. chim.* **1** (1882), 55.
A. Etard. *Compt. rend.* **114** (1892), 112 [*Zentr.* **1892 I**, 373].
J. W. Retgers. *Z. anorg. Chem.* **3** (1893), 252 [*Zentr.* **1893 I**, 923].
M. Dukelski. *Z. anorg. Chem.* **53** (1907), 327 [*C. A.* **1**, 2209].
218. Armin Seidenberg. *J. Am. Chem. Soc.* **43** (1921), 1325.
219. W. H. Krug and K. P. McElroy. *J. Anal. Chem.* **6** (1892), 184.
220. Alex. Naumann. *Ber.* **32** (1899), 999.
221. Alex. Naumann. *Ber.* **37** (1904), 4328.
222. Alex. Naumann. *Ber.* **37** (1904), 3600; **43** (1910), 313 [*C. A.* **4**, 1851].

223. Alex. Naumann. *Ber.* **37** (1904), 4608.

224. Alex. Naumann. *Ber.* **42** (1909), 3789 [*C. A.* **4**, 533].

225. Alex. Naumann. *Ber.* **47** (1914), 247 [*C. A.* **8**, 1373].

226. Alex. Naumann. *Ber.* **47** (1914), 1369 [*C. A.* **8**, 3649].

227. A. Bourgom. *Bull. soc. chim. Belg.* **33** (1924), 101 [*C. A.* **18**, 1814].

228. Wilhelm Eidmann. *Zentr.* **1899 II**, 1014.

229. M. Stuckgold. *J. chim. phys.* **15** (1917), 505 [*C. A.* **12**, 876].

230. Franz Sachs. *Ber.* **34** (1901), 497.

231. L. Péan de St. Gilles. *Ann. chim. phys.* [3] **55** (1859), 396.

232. A. E. Hill. *J. Am. Chem. Soc.* **43** (1921), 263.

233. C. A. Lobry de Bruyn. *Rec. trav. chim.* **11** (1892), 112; *Z. physik. Chem.* **10** (1892), 782; *Ber.* **26** (1893), 268 [*Zentr.* **1893 I**, 296, 599].

234. Atherton Seidell. "Solubilities of Inorganic and Organic Compounds" (Van Nostrand, New York, 1919).

235. W. E. S. Turner and C. C. Bissett. *J. Chem. Soc.* **103** (1913), 1904 [*C. A.* **8**, 853].

236. C. A. Lobry de Bruyn. *Z. physik. Chem.* **10** (1892), 782 [*Zentr.* **1893 I**, 296].

237. W. Herz and F. Kuhn. *Z. anorg. Chem.* **60** (1908), 152 [*C. A.* **3**, 856].

238. H. E. Patten and W. R. Mott. *J. Phys. Chem.* **8** (1904), 157 [*Zentr.* **1904 I**, 1474].

239. M. Centnerszwer. *Z. physik. Chem.* **72** (1910), 431 [*C. A.* **4**, 1831].

240. J. Dumas and E. Peligot. *Ann. chim. phys.* [2] **58** (1835), 5.

241. P. P. von Veimarn. *J. Russ. Phys.-Chem. Soc.* **40** (1908), 1126 [*C. A.* **3**, 307].

242. A. Gerardin. *Ann. chim. phys.* [4] **5** (1865), 129.

243. Hugo Schiff. *Ann.* **118** (1861), 365.

244. A. Klepl. *J. prakt. Chem.* [2] **25** (1882), 526 [*Zentr.* **1882**, 619].

245. de Forcrand. *Compt. rend.* **102** (1886), 551 [*Zentr.* **1886**, 305].

246. S. E. Simon. *J. prakt. Chem.* [2] **20** (1879), 371 [*Zentr.* **1879**, 805].

247. H. A. Curtis and R. M. Burns. *J. Am. Chem. Soc.* **39** (1917), 33.

248. Geo. Pucher and W. M. Dehn. *J. Am. Chem. Soc.* **43** (1921), 1753.

249. W. Herz and M. Knoch. *Z. anorg. Chem.* **41** (1904) 315 [*Zentr.* **1904 II**, 1182].

250. W. Herz and M. Knoch. *Z. anorg. Chem.* **45** (1905) 262 [*Zentr.* **1905 II**, 93].

251. W. Herz and M. Knoch. *Z. anorg. Chem.* **46** (1905) 193 [*Zentr.* **1905 II**, 956].

252. W. Herz and G. Anders. *Z. anorg. Chem.* **55** (1907) 271 [*C. A.* **1**, 2856].

253. W. Herz and G. Anders. *Z. anorg. Chem.* **52** (1907) 164 [*C. A.* **1**, 955].

254. W. Herz and F. Kuhn. *Z. anorg. Chem.* **58** (1908) 159 [*C. A.* **2**, 2638].

255. Hans Malfatti. *Z. anal. Chem.* **50** (1911), 692 [*C. A.* **6**, 200].

256. S. T. McCallum. *J. Ind. Eng. Chem.* **13** (1921), 943.

257. M. Scholtz. *Arch. Pharm.* **236** (1898), 533; **237** (1899), 199 [*Zentr.* **1898 II**, 983; **1899 I**, 1245].

258. W. R. Orndorff and J. J. Kennedy. *J. Am. Chem. Soc.* **39** (1917), 91.

259. T. H. Reade and S. A. Sim. *J. Chem. Soc.* **125** (1924), 157 [*C. A.* **18**, 977].

260. S. Ruhemann. *Ber.* **54** (1921), 2565 [*C. A.* **16**, 636].

261. Hans Stäger. *Helvetica Chim. Acta* **6** (1923), 893 [*C. A.* **18**, 164].

262. Emil Knoevenagel. *Ber.* **23** (1890), 2995.

263. E. B. Holland. *J. Ind. Eng. Chem.* **3** (1911), 172.

264. W. H. Emerson and H. N. Dumas. *J. Am. Chem. Soc.* **31** (1909), 949.

265. E. R. Bishop *et al.* *J. Am. Chem. Soc.* **44** (1922), 135.

266. Lassar-Cohn. *Z. physiol. Chem.* **16** (1892), 497 [*Zentr.* **1892 II**, 247]; *Ber.* **25** (1892), 805.

267. Leopold Semper and Leo Lichtenstadt. *Ann.* **400** (1913), 321 [*C. A.* **8**, 63].
268. C. L. Jackson and S. A. Beggs. *J. Am. Chem. Soc.* **38** (1916), 677.
269. Heinrich Biltz. *Ann.* **368** (1909), 180 [*C. A.* **4**, 307].
270. Torsten Swensson. *Z. wiss. Phot.* **20** (1921), 206 [*C. A.* **15**, 2838].
271. Fredk. Stanbridge. *J. Chem. Soc.* **113** (1918), 808 [*C. A.* **13**, 577].
272. O. Hesse. *J. prakt. Chem.* [2] **64** (1901), 361 [*Zentr.* **1901 II**, 1313].
273. A. F. Holleman and A. C. Antusch. *Rec. trav. chim.* **13** (1894), 288 [*Zentr.* **1895 I**, 523].
274. Richard Willstätter. *J. Am. Chem. Soc.* **37** (1915), 335.
275. F. Mylius. *Ber.* **20** (1887), 1970.
276. N. V. Sidgwick and W. J. Spurrell. *J. Chem. Soc.* **117** (1920), 1404 [*C. A.* **15**, 332].
277. H. C. Wood, Jr. *J. Am. Pharm. Assoc.* **9** (1920), 878 [*C. A.* **15**, 926].
278. J. L. Somerville. *C. A.* **16**, 3525; *Zentr.* **1923 II**, 580.
279. H. Kiliani. *Ber.* **24** (1891), 339; *Arch. Pharm.* **231** (1893), 460 [*Zentr.* **1893 II**, 327].
280. B. A. Hunt. *J. Chem. Soc.* **117** (1920), 1593 [*C. A.* **15**, 1019].
281. R. A. Hall. *J. Am. Chem. Soc.* **37** (1915), 213.
282. H. Kiliani. *Arch. Pharm.* **233** (1895), 302 [*Zentr.* **1895 II**, 367].
283. A. L. Macleod *et al.* *J. Am. Chem. Soc.* **44** (1922), 2263.
284. H. Biedermann. *Arch. Pharm.* **221** (1883), 181 [*Zentr.* **1883**, 265].
285. Franz Hoffmeister. *Ann.* **189** (1877), 16 [*Zentr.* **1877**, 817].
286. W. A. Noyes and W. F. Goebel. *J. Am. Chem. Soc.* **44** (1922), 2287.
287. Lassar-Cohn. *Ber.* **27** (1894), 1340; *Z. physiol. Chem.* **19** (1894), 564 [*Zentr.* **1894 II**, 525].
288. H. Führer. *Ber.* **57**B (1924), 512 [*C. A.* **18**, 2493].
289. T. G. Thompson *et al.* *J. Am. Chem. Soc.* **43** (1921), 879.
290. N. S. Osborne and E. C. McKelvy. *Bur. Standards Bull.* **9** (1913), 436 [*C. A.* **7**, 2889].
291. W. Plücker. *Z. Nahr. Genussm.* **17** (1909), 454 [*C. A.* **3**, 2032].
292. Georges Patart. *Bull. soc. encour. ind. nat.* **136** (1924), 201 [*C. A.* **18**, 2405].
293. René Pique. *Bull. assoc. chim. sucr. dist.* **41** (1924), 337, 386 [*C. A.* **18**, 3097].
294. Sidney Young and E. C. Fortey. *J. Chem. Soc.* **81** (1902), 719.
295. Calculated from Young and Fortey's data with the aid of *Bur. Standards Circ.* No. **19** (1916), p. 19.
296. Roger Adams and C. S. Marvel. *J. Am. Chem. Soc.* **43** (1921), 317.
297. A. W. Dox and Lester Yoder. *J. Am. Chem. Soc.* **43** (1921), 681.
298. N. A. Shepard and A. A. Ticknor. *J. Am. Chem. Soc.* **38** (1916), 385.
299. W. M. Fischer. *Z. physik. Chem.* **92** (1918), 587 [*C. A.* **12**, 2154].
300. Chas. Caspari, Jr. *Am. J. Pharm.* **68** (1896), 473.
301. L. F. Kebler. *Am. J. Pharm.* **68** (1896), 667.
302. T. Lowitz and D. Richter. Cited by N. S. Osborne and E. C. McKelvy *Bur. Standards Bull.* **9** (1913), 330 [*C. A.* **7**, 2889].
303. E. Soubeiran. *Ann.* **30** (1839), 356.
304. Christian Göttig. *Ber.* **23** (1890), 181.
305. D. Mendeleeff. *Z. Chem.* **8** (1865), 257; *Phil. Mag.* [4] **31** (1866), 137 [*Zentr.* **1866**, 224]. See also *Ann. Physik. Chem.* [5] **18** (1869), 239.
306. M. D. Mann. U. S. 1,452,206 (1923) [*C. A.* **17**, 1968].
307. J. A. S. Hammond. U. S. 1,466,435 (1923); Reissue 15,783 (1924) [*C. A.* **17**, 3881; **18**, 1300].

308. Sidney Young. "Distillation Principles and Processes" (Macmillan, London, 1922), p. 37.
309. W. H. Perkin. *J. Chem. Soc.* **45** (1884), 465.
310. Luigi Solari. Fr. 484,323 (1917) [*C. A.* **12**, 1050; **11**, 2807].
311. R. B. Lebo. *J. Am. Chem. Soc.* **43** (1921), 1005.
312. J. H. Hess. U. S. 996,763 (1911) [*C. A.* **5**, 2692].
313. P. Verola *et al.* Brit. 210,432 (1924) [*C. A.* **18**, 1729].
314. Robert Kane. *Ann.* **19** (1836), 164.
315. G. B. Frankforter and F. C. Frary. *J. Phys. Chem.* **17** (1913), 405 [*C. A.* **7**, 2176]. G. B. Frankforter. U. S. 1,350,254 (1920) [*C. A.* **14**, 3294].
316. G. B. Frankforter. U. S. 1,350,254 (1920) [*C. A.* **14**, 3294].
317. Brit. 206,516 (1923) [*C. A.* **18**, 1191].
318. Edmund Knecht and E. F. Muller. *J. Soc. Chem. Ind.* **43** (1924), 177T [*C. A.* **18**, 2494].
319. C. Mariller. *Chimie et industrie* **10** (1923), 643 [*C. A.* **18**, 375]. See also C. Mariller and van Ruymbeke. *Compt. rend.* **175** (1922), 588 [*C. A.* **17**, 332].
320. Joseph van Ruymbeke. Brit. 184,036 (1922), 184,129 (1922) [*C. A.* **17**, 770]; U. S. 1,459,699 (1923), 1,474,216 (1923) [*C. A.* **17**, 2715; **18**, 537]. See also René Pique. *Bull. assoc. chim. sucr. dist.* **41** (1924) 347 [*C. A.* **18**, 3097].
321. Joseph Schneible. U. S. 1,469,447 (1923) [*C. A.* **17**, 3904].
322. R. F. Brunel *et al.* *J. Am. Chem. Soc.* **43** (1921), 568.
323. J. L. Smith. *Am. Chemist* **5** (1875), 120 [see *Zentr.* **1875**, 103].
324. Brit. 189,136 (1921) [*C. A.* **18**, 565].
325. René Pique. *Bull. assoc. chim. sucr. dist.* **41** (1924), 351 [*C. A.* **18**, 3097].
326. Anton Kailan. *Monatsh.* **28** (1907), 927 [*Zentr.* **1907 II**, 1489].
327. W. A. Noyes. *J. Am. Chem. Soc.* **45** (1923), 860.
328. W. H. Warren. *J. Am. Chem. Soc.* **32** (1910), 698.
329. Emil Erlenmeyer. *Ann.* **160** (1871), 249.
330. E. P. Wightman *et al.* *J. Am. Chem. Soc.* **36** (1914), 2246.
331. L. W. Andrews. *J. Am. Chem. Soc.* **30** (1908), 353.
332. E. R. Squibb. *Chem. News* **51** (1885), 7, 21, 31.
333. E. R. Squibb. *J. Am. Chem. Soc.* **15** (1893), 133.
334. P. S. Danner and J. H. Hildebrand. *J. Am. Chem. Soc.* **44** (1922), 2826.
335. H. S. Harned and M. H. Fleysher. *J. Am. Chem. Soc.* **47** (1925), 83.
336. N. S. Osborne and E. C. McKelvy. *Bur. Standards Bull.* **9** (1913), 329 [*C. A.* **7**, 2889].
337. L. Crismer. *Bull. soc. chim. Belg.* **18** (1904), 18 [*Zentr.* **1904 I**, 1479].
338. Joseph Gyr. *Ber.* **41** (1908), 4325 [*C. A.* **3**, 651].
339. John Johnston. *J. Am. Chem. Soc.* **30** (1908), 1361.
340. John Johnston. *Z. physik. Chem.* **62** (1908), 341 [*C. A.* **2**, 2033].
341. Fr. v. Konek. *Ber.* **39** (1906), 2264.
342. M. Berthelot and L. Pean de St. Gilles. *Jahresber.* **15** (1862), 392.
343. W. A. Noyes and R. R. Warfel. *J. Am. Chem. Soc.* **23** (1901), 464
344. A. N. Cook and A. L. Haines. *Proc. Iowa Acad. Sci.* **9** (1901), 86 [*J. Am. Chem. Soc.* **25** (1903), R559].
345. C. Vincent and Delachenal. *Compt. rend.* **90** (1880), 1360 [*Zentr.* **1880**, 469].
346. L. W. Winkler. *Ber.* **38** (1905), 3612.

347. H. Goldschmidt and Einar Sunde. *Ber.* **39** (1906), 711.

348. Arthur Lapworth and J. R. Partington. *J. Chem. Soc.* **97** (1910), 24 [*C. A.* **4**, 1127].

349. P. Loriette. Brit. 189,453 (1922) [*C. A.* **17**, 2470].

350. F. M. Perkin and Lionel Pratt. *Proc. Chem. Soc.* **23** (1907), 304 [*C. A.* **2**, 993].

351. N. S. Osborne *et al.* *J. Wash. Acad. Sci.* **2** (1912), 95 [*C. A.* **6**, 1085].

352. Henri Moissan. *Compt. rend.* **127** (1898), 499 [*Zentr.* **1898 II**, 960].

353. L. W. Winkler. *Z. angew. Chem.* **29** (1916), Aufsatzteil 18 [*C. A.* **10**, 1187].

354. Heinrich Goldschmidt and Arthur Thuesen. *Z. physik. Chem.* **81** (1912), 31 [*C. A.* **7**, 1651].

355. Heinrich Goldschmidt. *Z. physik. Chem.* **89** (1914), 130 [*C. A.* **9**, 745].

356. Brit. 21,567 (1906) [*C. A.* **1**, 945], Ger. 175,780 (1906) [*C. A.* **1**, 1203].

357. H. C. Robertson and S. F. Acree. *Am. Chem. J.* **49** (1913), 494 [*C. A.* **7**, 3125].

358. Peter Klason and Evert Norlin. *J. Chem. Soc. Abstr.* **90** (1906) i, 921; *Zentr.* **1906 II**, 1480.

359. Niels Bjerrum and László Zechmeister. *Ber.* **56**B (1923), 894 [*C. A.* **17**, 2701].

360. Anton Kailan. *Monatsh.* **27** (1906), 546 [*Zentr.* **1906 II**, 777].

361. H. Goldschmidt. *Atti VI Cong. internaz. chim. applicata* (1906) **6**, 159.

362. F. G. Keyes and W. J. Winninghoff. *J. Am. Chem. Soc.* **38** (1916), 1179.

363. C. A. Kraus and J. E. Bishop. *J. Am. Chem. Soc.* **44** (1922), 2207.

364. C. S. Marvel and A. L. Tanenbaum. *J. Am. Chem. Soc.* **44** (1922), 2646.

365. E. C. McKelvy and D. H. Simpson. *J. Am. Chem. Soc.* **44** (1922), 109.

366. L. Claisen. *Ber.* **40** (1907), 3906 [*C. A.* **2**, 94].

367. C. Friedel and J. M. Crafts. *Ann. chim. phys.* [4] **9** (1866), 35.

368. Hans Wislicenus and Ludwig Kaufmann. *Ber.* **28** (1895), 1324.

369. Hans Wislicenus. *J. prakt. Chem.* [2] **54** (1896), 55 [*Zentr.* **1896 II**, 772].

370. Emm. Pozzi-Escot. *Bull. assoc. chim. sucr. dist.* **26** (1909), 580 [*C. A.* **3**, 1199].

371. W. W. Clough and C. O. Johns. *Ind. Eng. Chem.* **15** (1923), 1031.

372. Homer Adkins. *J. Am. Chem. Soc.* **44** (1922), 2178.

373. Thos. Evans and W. C. Fetsch. *J. Am. Chem. Soc.* **26** (1904), 1160.

374. C. N. Riiber. *Z. Elektrochem.* **29** (1923), 336 [*C. A.* **17**, 3434].

375. Thv. Lindemann. *C. A.* **7**, 2359.

376. P. Yvon. *Compt. rend.* **125** (1897), 1181 [*Zentr.* **1898 I**, 319].

377. G. B. Frankforter. U. S. 1,350,254 (1920) [*C. A.* **14**, 3294].

378. Sidney Young. Ref. 308, p. 194.

379. René Pique. *Bull. assoc. chim. sucr. dist.* **41** (1924), 398ff [*C. A.* **18**, 3097].

380. J. A. LeBel. *Compt. rend.* **88** (1879), 912 [*Zentr.* **1879**, 459].

381. John Wade and R. W. Merriman. *J. Chem. Soc.* **99** (1911), 997 [*C. A.* **5**, 2996].

382. R. W. Merriman. *J. Chem. Soc.* **103** (1913), 635 [*C. A.* **7**, 2546].

383. René Pique. *Bull. assoc. chim. sucr. dist.* **41** (1924), 407 [*C. A.* **18**, 3097].

384. Sidney Young. *J. Chem. Soc.* **81** (1902), 707; Ger. 142,502 (1903).

385. J. A. Steffens. Can. 234,340 (1923) [*C. A.* **17**, 3566]; U. S. 1,490,520 (1924) [*C. A.* **18**, 2055].

386. E. C. R. Marks. Brit. 213,984 (1923) [*C. A.* **18**, 2578].

387. A. A. Backhaus. U. S. 1,508,435 (1924) [*C. A.* **19**, 78].

388. *Zentr.* **1924 II**, 1863.

389. E. C. R. Marks. Brit. 213,985 (1923) [*C. A.* **18**, 2578]; see also Brit. 211,454 (1924) [*C. A.* **18**, 2055].

390. W. H. Rodebush. Can. 234,338 (1923) [*C. A.* **17**, 3566]; U. S. 1,487,182 (1924) [*C. A.* **18**, 1729].
391. Brit. 215,716 (1923) [*C. A.* **18**, 2929].
392. G. Chavanne, *Bull. soc. chim. Belg.* **27** (1913), 205 [*C. A.* **8**, 1105].
393. Henri Guinot. *Compt. rend.* **176** (1923), 1623 [*C. A.* **17**, 2578].
394. Edouard and Remy Urbain. *Compt. rend.* **176** (1923), 166 [*C. A.* **17**, 1566].
395. Joseph Gyr. *Ber.* **41** (1908), 4311 [*C. A.* **3**, 651].
396. H. Goldschmidt. *Ber.* **28** (1895), 3222; **39** (1906), 719.
397. Anton Kailan. *Ber.* **44** (1911), 2884 [*C. A.* **6**, 232].
398. G. Bredig and W. Fraenkel. *Ber.* **39** (1906), 1756.
399. G. Bredig and W. Fraenkel. *Z. Elektrochem.* **11** (1905), 525 [*Zentr.* **1905 II**, 805].
400. L. Crismer. *Bull. soc. chim. Belg.* **17** (1903), 180; **18** (1904), 18; **20** (1906), 294 [*Zentr.* **1904 I**, 1479; **1907 I**, 1068. See also *Zentr.* **1902 II**, 3; *Bull. soc. chim.* **29** (1903), 719].
401. E. C. McKelvy and D. H. Simpson. *J. Am. Chem. Soc.* **44** (1922), 105.
402. K. J. P. Orton and D. C. Jones. *J. Chem. Soc.* **115** (1919), 1057 [*C. A.* **14**, 114].
403. L. Crismer. *Bull. soc. chim. Belg.* **14** (1900), 346.
404. I. M. Kolthoff. *C. A.* **17**, 1774; *Bull. assoc. chim. sucr. dist.* **41** (1924), 374.
405. E. Waller. *J. Am. Chem. Soc.* **11** (1889), 124.
406. Mejer Wildermann. *Z. physik. Chem.* **14** (1894), 232 [*Zentr.* **1894 II**, 188].
407. F. L. Dunlap. *J. Am. Chem. Soc.* **28** (1906), 395.
408. A. W. Rowe and E. P. Phelps. *J. Am. Chem. Soc.* **46** (1924), 2078.
409. Quoted by S. A. Vasey in "Guide to the Analysis of Potable Spirits" (Baillière, Tindall & Cox, London, 1904), p. 22, as found in "Manuel Pratique de l'Analyse des Alcohols et des Spiriteux" by Girard and Cuniasse (Masson et Cie., Paris).
410. W. Windisch. *Z. anal. Chem.* **27** (1888), 514 [*Zentr.* **1887**, 468].
411. Herman Heuser. U. S. 1,498,274 (1924) [*C. A.* **18**, 3194].
412. Joseph Paul. *Z. anal. Chem.* **35** (1896), 648 [*Zentr.* **1897 I**, 488].
413. A. Castille and Victor Henri. *Bull. soc. chim. biol.* **6** (1924), 299 [*C. A.* **18**, 3165].
414. A. Lanzenberg and J. Duclaux. *Bull. soc. chim.* [4] **29** (1921), 135 [*C. A.* **15**, 2061].
415. R. C. Menzies. *J. Chem. Soc.* **121** (1922), 2790 [*C. A.* **17**, 970].
416. C. A. Carlton. *J. Am. Chem. Soc.* **44** (1922), 1471.
417. P. Loriette. *Chimie et industrie,* Spec. No. (May, 1923), p. 718 [*C. A.* **17**, 3241].
418. G. O. Curme, Jr., and E. W. Reid. *Chem. Met. Eng.* **25** (1921), 1050 [*C. A.* **16**, 2107].
419. L. W. Winkler. *Z. angew. Chem.* **24** (1911), 636 [*C. A.* **5**, 2340].
420. D. H. Grant and C. O. Johns. *Am. J. Pharm.* **94** (1922), 418 [*C. A.* **16**, 2944].
421. H. C. Fuller. *Chem. Met. Eng.* **29** (1923), 538 [*C. A.* **17**, 3745].
422. M. Heidelberger and W. A. Jacobs. *J. Am. Chem. Soc.* **41** (1919), 2138.
423. Hans Lecher and Josef Hofmann. *Ber.* **55**B (1922), 912 [*C. A.* **16**, 3598].
424. C. D. Hurd and H. J. Brownstein. *J. Am. Chem. Soc.* **47** (1925), 67.
425. Pépin-Lehalleur. *Ann. chim. anal. chim. appl.* [2] **3** (1921), 361 [*C. A.* **16**, 1690].
426. A. M. Pardee *et al.* *J. Ind. Eng. Chem.* **12** (1920), 129, 481.

427. G. F. Smith. *J. Am. Chem. Soc.* **45** (1923), 2072.
428. H. D. Dakin. *Biochem. J.* **12** (1918), 293 [*C. A.* **13**, 1478].
429. P. Latschinow. *Ber.* **20** (1887), 3275.
430. A. Michael *et al.* *J. Am. Chem. Soc.* **38** (1915), 663.
431. K. J. P. Orton and D. C. Jones. *J. Chem. Soc.* **115** (1919), 1198 [*C. A.* **14**, 370].
432. R. B. Lebo. U. S. 1,422,583 (1922) [*C. A.* **16**, 3093].
433. W. Küster. *Ber.* **27** (1894), 573.
434. M. Nencki and N. Sieber. *Arch. exptl. Path. Pharmakol.* **20** (1886), 328 [*Zentr.* **1886**, 886].
435. Stefan von Niementowski. *J. prakt. Chem.* [2] **40** (1889), 22 [*Zentr.* **1889 II**, 331].
436. L. von Uslar and J. Erdmann. *Ann.* **120** (1861), 121.
437. G. D. Beal and T. S. Hamilton. *J. Am. Pharm. Assoc.* **9** (1920), 14 [*C. A.* **14**, 1004].
438. F. Klingemann and W. F. Laycock. *Ber.* **24** (1891), 513.
439. D. L. Hammick and G. H. Locket. *J. Chem. Soc.* **121** (1922), 2363 [*C. A.* **17**, 548].
440. H. Hartridge. *J. Physiol.* **54** (1920), *Proc. Physiol. Soc.* viii [*C. A.* **15**, 2463].
441. A. J. J. Vandevelde. *Bull. soc. chim. Belg.* **30** (1921), 16 [*C. A.* **15**, 3779].
442. F. Mylius. *Ber.* **19** (1886), 373.
443. G. O. Curme, Jr., and C. O. Young. *Chem. Met. Eng.* **28** (1923), 169 [*C. A.* **17**, 1427].
444. H. C. Fuller. *Ind. Eng. Chem.* **16** (1924), 624.
445. Klever. *Bull. soc. chim.* [3] **18** (1872), 372 [*Zentr.* **1872**, 434].
446. A. M. Ossendovsky. *J. Russ. Phys.-Chem. Soc.* **37** (1906), 1071 [*C. A.* **1**, 1386].
447. K. Holm. *C. A.* **15**, 2962, 3181.
448. C. Mariller. *Chimie et industrie* **10** (1923), 644 [*C. A.* **18**, 375].
449. W. Herz and M. Knoch. *Z. anorg. Chem.* **45** (1905), 266 [*Zentr.* **1905 II**, 93].
450. Ger. 141,976 (1903); *Frd.* **VII**, 36; *Win.* **I**, 54.
451. Hugo Erdmann. *Ann.* **275** (1893), 258 [*Zentr.* **1893 II**, 268].
452. Godfrin. *J. pharm. chim.* [7] **2** (1910), 387 [*C. A.* **5**, 2300].
453. Ger. 46,252 (1888); *Frd.* **II**, 373; *Win.* **II**, 1218.
454. A. G. Green. *J. Chem. Soc.* **89** (1906), 1602; *J. Soc. Dyers Colourists* **23** (1907), 162.
455. Ger. 49,844 (1889); *Frd.* **II**, 177; *Win.* **II**, 434.
456. Br. Pawlewski. *Ber.* **27** (1894), 1566.
457. Johannes Thiele and Otto Dimroth. *Ber.* **28** (1895), 1412.
458. H. Flemming. *Chem. Ztg.* **21** (1897), 97 [*Zentr.* **1897 I**, 539].
459. Brit. 193,521 (1921) [*C. A.* **17**, 3416].
460. L. H. Friedburg. *J. Am. Chem. Soc.* **12** (1890), 288.
461. O. Wallach and W. Brass. *Ann.* **225** (1884), 295 [*Zentr.* **1884**, 900].
462. L. Valli-Douau. *C. A.* **19**, 703.
463. U. S. P. IX (1916), p. 32.
464. Charles Baskerville and W. A. Hamor. *J. Ind. Eng. Chem.* **3** (1911), 302.
465. A. M. Clover. *J. Am. Chem. Soc.* **44** (1922), 1107; **46** (1924), 419.
466. A. W. Rowe. *Ind. Eng. Chem.* **16** (1924), 896.
467. Lassar-Cohn. *Ann.* **284** (1895), 226 [*Zentr.* **1895 I**, 561].
468. Lassar-Cohn. "Application of some General Reactions to Investigations in Organic Chemistry," trans. by J. B. Tingle (Wiley, New York, 1904), p. 24.

469. R. S. Taylor and L. B. Smith. *J. Am. Chem. Soc.* **44** (1922), 2455.
470. R. K. Newman. *J. Soc. Chem. Ind.* **43** (1924), 287T [*C. A.* **19**, 24].
471. J. Durand. *Compt. rend.* **172** (1921), 70 [*C. A.* **15**, 1282].
472. J. A. S. Hammond. U. S. 1,466,436 (1923) [*C. A.* **17**, 3881].
473. John Wade and Horace Finnemore. *J. Chem. Soc.* **95** (1909), 1842 [*C. A.* **4**, 702].
474. E. von Siebenrock. *Monatsh.* **30** (1909), 759 [*C. A.* **4**, 1400].
475. Henry Gilman and N. J. Beaber. *J. Am. Chem. Soc.* **47** (1925), 522.
476. J. U. Nef. *Ann.* **287** (1895), 332 [*Zentr.* **1895 II**, 637].
477. Th. Poleck and K. Thümmel. *Ber.* **22** (1889), 2863.
478. G. Guérin. *J. pharm. chim.* [7] **6** (1912), 212 [*C. A.* **7**, 1261].
479. Gustavus Michaelis. U. S. 1,189,602 (1916) [*C. A.* **10**, 2125].
480. E. M. Flaherty. U. S. 1,312,475 (1919) [*C. A.* **13**, 2575].
481. L. van Itallie and J. E. van der Zande. *C. A.* **10**, 1906; *Zentr.* **1916 I**, 1277.
482. K. Feist. *C. A.* **4**, 1895; *Zentr.* **1910 I**, 1166.
483. J. Herzog. *C. A.* **8**, 1186; *Zentr.* **1914 I**, 806.
484. Charles Baskerville and W. A. Hamor. *J. Ind. Eng. Chem.* **3** (1911), 395.
485. G. B. Frankforter and E. A. Daniels. *J. Am. Chem. Soc.* **37** (1915), 2565.
486. O. Maass and D. McIntosh. *J. Am. Chem. Soc.* **34** (1912), 1275.
487. G. S. Forbes and A. S. Coolidge. *J. Am. Chem. Soc.* **41** (1919), 152.
488. P. W. Carleton. *J. Am. Chem. Soc.* **38** (1916), 1134.
489. E. and H. Salkowski. *Z. physiol. Chem.* **7** (1882–3), 162 [*Zentr.* **1883**, 561].
490. Partheil and Rose. *Ber.* **34** (1901), 3611.
491. Hugo Schiff. *Ann.* **229** (1885), 373 [*Zentr.* **1885**, 729]; *Z. physik. Chem.* **23** (1897), 355 [*Zentr.* **1897 II**, 250].
492. Morris Loeb. *J. Am. Chem. Soc.* **27** (1905), 1019.
493. Erwin Voit. *Z. Biol.* **35** (1897), 566.
494. G. Cusmano and E. Cattini. *Gazz. chim. ital.* **54** (1924), 383 [*C. A.* **19**, 56].
495. M. T. Bogert and Alfred Hoffmann. *J. Am. Chem. Soc.* **27** (1905), 1294.
496. A. G. Perkin. *J. Chem. Soc.* **117** (1920), 701 [*C. A.* **14**, 3221].
497. P. Jannasch and A. Rathjen. *Ber.* **32** (1899), 2391.
498. Marcel Descudé. *Compt. rend.* **132** (1901), 1129 [*Zentr.* **1901 I**, 1265].
499. E. Wedekind and J. Haussermann. *Ber.* **34** (1901), 2081.
500. Edgar Wedekind. *Ber.* **34** (1901), 2073.
501. M. Berthelot. *Ann.* **92** (1854), 352.
502. J. E. Darrah and C. G. MacArthur. *J. Am. Chem. Soc.* **38** (1916), 922.
503. Lassar-Cohn. Ref. 91, p. 12.
504. Ger. 70,813 (1893); *Frd.* **III**, 995; *Win.* **II**, 1201.
505. E. Schär. *Arch. Pharm.* **225** (1887), 623 [*Zentr.* **1887**, 1100].
506. J. W. Brühl. *Ber.* **28** (1895), 2858.
507. Ludwig Knorr *et al.* *Ber.* **44** (1911), 1143 [*C. A.* **5**, 2837].
508. W. H. Perkin, Jr., and Robert Robinson. *J. Chem. Soc.* **103** (1913), 1984 [*C. A.* **8**, 909].
509. R. Gnehm and F. Kaufler. *Ber.* **37** (1904), 3032.
510. L. Hugounenq. *J. pharm. chim.* [6] **4** (1896), 447 [*Zentr.* **1897 I**, 61].
511. Th. Zerewitinoff. *Ber.* **43** (1910), 3593 [*C. A.* **5**, 1285].
512. K. J. P. Orton *et al.* *J. Chem. Soc.* **99** (1911), 1178 [*C. A.* **5**, 3561].
513. K. J. P. Orton and A. E. Bradfield. *J. Chem. Soc.* **125** (1924), 960 [*C. A.* **18**, 2127].

514. W. R. Bousfield and T. M. Lowry. *J. Chem. Soc.* **99** (1911), 1435 [*C. A.* **5**, 3568].
515. E. R. Squibb. *Am. J. Pharm.* **71** (1899), 1, 305; **72** (1900), 1, 311 [*Zentr.* **1900 I**, 354].
516. R. Willstätter and E. K. Bolton. *Ann.* **412** (1916), 119 [*C. A.* **11**, 1404].
517. M. T. Bogert and W. F. Hand. *J. Am. Chem. Soc.* **27** (1905), 1478.
518. J. H. Schmidt. *J. Am. Chem. Soc.* **43** (1921), 2452.
519. Ryuji Abe. *Mem. Coll. Sci. Eng. Kyoto Imp. Univ.* **3** (1911), 13 [*C. A.* **5**, 2820].
520. T. B. Johnson and G. C. Bailey. *J. Am. Chem. Soc.* **38** (1916), 2141.
521. C. Gastalde. *Gazz. chim. ital.* **51 II** (1921), 300 [*C. A.* **16**, 1411].
522. J. R. Bailey and R. H. Pritchett. *J. Am. Chem. Soc.* **40** (1918), 1230.
523. J. R. Bailey *et al.* *J. Am. Chem. Soc.* **37** (1915), 940; **38** (1916), 1784; **39** (1917), 279.
524. Richard Willstätter and Daniel Jaquet. *Ber.* **51** (1918), 774 [*C. A.* **13**, 577].
525. W. L. Lewis and C. S. Hamilton. *J. Am. Chem. Soc.* **45** (1923), 760.
526. H. W. Underwood, Jr., and E. L. Kochmann. *J. Am. Chem. Soc.* **45** (1923), 3073.
527. A. S. Wheeler and I. W. Smithey. *J. Am. Chem. Soc.* **43** (1921), 2613.
528. August Wernicke and Wilhelm Pfitzinger. Ger. 20,595 (1882); U. S. 260,340 (1882); *Ber.* **15** (1882), 3105.
529. C. S. Hudson and H. L. Sawyer. *J. Am. Chem. Soc.* **39** (1917), 473.
530. C. S. Hudson and J. K. Dale. *J. Am. Chem. Soc.* **39** (1917), 322.
531. A. W. Mangam and S. F. Acree. *J. Am. Chem. Soc.* **39** (1917), 966.
532. E. G. Griffin and J. M. Nelson. *J. Am. Chem. Soc.* **37** (1915), 1555.
533. T. S. Harding. *J. Am. Chem. Soc.* **44** (1922), 1766.
534. H. I. Schlesinger and R. P. Calvert. *J. Am. Chem. Soc.* **33** (1911), 1924.
535. H. I. Schlesinger and A. W. Martin. *J. Am. Chem. Soc.* **36** (1914), 1590.
536. E. R. Schierz. *J. Am. Chem. Soc.* **45** (1923), 447.
537. J. B. Garner *et al.* *Am. Chem. J.* **46** (1911), 238 [*C. A.* **5**, 3681].
538. M. C. Boswell and H. E. Corman. *Can. Chem. Met.* **6** (1922), 64 [*C. A.* **16**, 1393].
539. Ossian Aschan. *Ann.* **271** (1892), 266 [*Zentr.* **1892 II**, 649].
540. Ossian Aschan. *Chem. Ztg.* **37** (1913), 1117 [*C. A.* **7**, 3873].
541. Remy and Erhart. Ger. 38,417 (1886); *Frd.* **I**, 304; *Win.* **I**, 941.
542. C. F. Mabery. *Ind. Eng. Chem.* **15** (1923), 1234.
543. André Dubosc. *Caoutchouc et gutta-percha* **15** (1918), 9555 [*C. A.* **14**, 3650].
544. L. Gattermann and A. Ritschke. *Ber.* **23** (1890), 1747.
545. J. H. Walton and L. L. Withrow. *J. Am. Chem. Soc.* **45** (1923), 2690.
546. Jenö Tausz. *Zentr.* **1919 IV**, 429.
547. Henry Dreyfus. U. S. 1,430,304 (1922) [*C. A.* **16**, 3903].
548. A. A. de Aguiar and Alex Bayer. *Ann.* **157** (1871), 367 [*Zentr.* **1871**, 265].
549. F. W. Heyl. *J. Am. Chem. Soc.* **44** (1922), 2285.
550. Iwan Ostromysslensky. *J. prakt. Chem.* [2] **76** (1907), 267 [*C. A.* **2**, 666].
551. P. Walden. *Bull. acad. sci. St. Petersburg* [6] **5** (1911), 1055 [*C. A.* **6**, 1394].
552. Erwin Ott and Bernhard Löpmann. *Ber.* **55**B (1922), 1258 [*C. A.* **16**, 3644].
553. A. F. O. Germann. *J. Phys. Chem.* **28** (1924), 879 [*C. A.* **18**, 3330].
554. Brit. 119,855 (1918) [*C. A.* **13**, 230].
555. Brit. 121,455 (1918) [*C. A.* **13**, 731].

556. W. H. Dawson. Brit. 174,784 (1920) [*C. A.* **16**, 1780].
557. F. W. Atack. U. S. 1,461,745 (1923) [*C. A.* **17**, 3033].
558. Ger. 158,500 (1905); *Frd.* **VII**, 782; *Win.* **II**, 542.
559. August Bernthsen. *Ann.* **251** (1889), 5 [*Zentr.* **1889 I**, 841].
560. O. N. Witt. *Ber.* **19** (1886), 2792.
561. J. H. Brègeat. U. S. 1,315,700–1 (1919) [*C. A.* **13**, 2983].
562. M. Roulleux and R. G. Dort. *Chem. Met. Eng.* **24** (1921), 916 [*C. A.* **15**, 2521].
563. A. A. Drummond. *J. Soc. Chem. Ind.* **40** (1921), 285T [*C. A.* **16**, 769].
564. H. Moschatos and B. Tollens. *Ann.* **272** (1893), 280 [*Zentr.* **1893 I**, 417].
565. H. Eckenroth. *Arch. Pharm.* **224** (1886), 624 [*Zentr.* **1886**, 672].
566. Willibald Henschel. *Ber.* **17** (1884), 1286.
567. P. Boessneck and O. Knoefler. *Ber.* **21** (1888), 782.
568. Georg Zierold. Ger. 61,551 (1890); *Frd.* **III**, 109; *Win.* **I**, 275.
569. W. Hoffmeister. *Ber.* **3** (1870), 748.
570. R. Hirsch. Ger. 58,001 (1890); *Frd.* **III**, 51; *Win.* **I**, 206
571. A. Pinner. *Ann.* **179** (1875), 68 [*Zentr.* **1876**, 164].
572. H. W. Matheson. Can. 223,597 (1922) [*C. A.* **16**, 3904].
573. Charles Baskerville and P. W. Cohen. *J. Ind. Eng. Chem.* **13** (1921), 334.
574. A. Michaelis. *Ber.* **15** (1882), 2876; *Ann.* **321** (1902), 160 [*Zentr.* **1902 II**, 42].
575. B. Phillips. *Ber.* **19** (1886), 1031.
576. W. J. Pope and E. E. Turner. *J. Chem. Soc.* **117** (1920), 1448 [*C. A.* **15**, 1493].
577. C. Etti. *Monatsh.* **1** (1880), 266.
578. J. W. T. Knox and A. B. Prescott. *J. Am. Chem. Soc.* **20** (1898), 45.
579. V. Wartha. *Ber.* **4** (1871), 334.
580. R. N. Riddle. U. S. 797,373 (1905).
581. J. W. Bruhl. *Ber.* **25** (1892), 1873.
582. S. Gabriel and Ernst Leupold. *Ber.* **31** (1898), 1278.
583. Koehler. *Zentr.* **1905 I**, 227.
584. H. Mann. *Zentr.* **1905 I**, 1231.
585. H. Mann. *Zentr.* **1905 I**, 812.
586. E. Knoevenagel and R. Weissgerber. *Ber.* **26** (1893), 439.
587. C. S. Miner *et al.* *Chem. Met. Eng.* **27** (1922), 299, 362 [*C. A.* **16**, 3894].
588. André Dubosc. *Caoutchouc et gutta-percha* **16** (1919), 9957 [*C. A.* **14**, 868].
589. C. E. Tharaldsen. *Science* **57** (1923), 305 [*C. A.* **17**, 1975].
590. Kathleen Shipsey and E. A. Werner. *J. Chem. Soc.* **103** (1913), 1255 [*C. A.* **7**, 3317].
591. Kathleen Shipsey and E. A. Werner. *Proc. Chem. Soc.* **29** (1913), 117.
592. H. L. Lochte *et al.* *J. Am. Chem. Soc.* **44** (1922), 2563.
593. J. Duclaux and A. Lanzenberg. *Bull. soc. chim.* [4] **27** (1920), 779 [*C. A.* **15**, 236].
594. G. B. Frankforter and Lillian Cohen. *J. Am. Chem. Soc.* **36** (1914), 1111.
595. Mitsumaru Tsujimoto. *C. A.* **15**, 1227; *J. Chem. Soc. Abstr.* **120** (1921) i, 78.
596. M. S. Kharasch and Lyman Chalkley, Jr. *J. Am. Chem. Soc.* **46** (1924), 1216.
597. G. N. Vis. Ger. 98,911 (1898); *Win.* **I**, 1259.
598. R. F. Remler. *Ind. Eng. Chem.* **15** (1923), 717; see also *C.A.* **19**, 1429.
599. Ernst Erdmann. Brit. 156,594 (1921).
600. Ernst Erdmann. Brit. 156,694 (1921) [*C. A.* **15**, 1804, 2720; see also *C. A.* **15**, 1808; **17**, 1322].
601. M. Gomberg. *J. Am. Chem. Soc.* **24** (1902), 601.

602. G. W. Pucher and T. B. Johnson. *J. Am. Chem. Soc.* **44** (1922), 823.
603. P. S. Varma and D. A. Kulkarni. *J. Am. Chem. Soc.* **47** (1925), 146.
604. LeRoy McMaster and A. C. Magill. *J. Am. Chem. Soc.* **38** (1916), 1789.
605. H. L. Lochte. *Ind. Eng. Chem.* **16** (1924), 956.
606. Otto Diels and Emil Abderhalden. *Ber.* **36** (1903), 3179.
607. W. A. Jacobs and Michael Heidelberger. *J. Am. Chem. Soc.* **41** (1919), 2106.
608. Emil Beringer. Ger. 104,106 (1899).
609. Ger. 78,861 (1894); *Frd.* **IV**, 270; *Win.* **I**, 942.
610. J. L. R. Morgan and O. M. Lammert. *J. Am. Chem. Soc.* **46** (1924), 884.
611. J. L. R. Morgan and O. M. Lammert. *J. Am. Chem. Soc.* **46** (1924), 1170.
612. J. L. R. Morgan and O. M. Lammert. *J. Am. Chem. Soc.* **46** (1924), 1117.
613. M. Scholtz. *Arch. Pharm.* **250** (1912), 423 [*C. A.* **7**, 211].
614. H. D. Gibbs. *J. Am. Chem. Soc.* **28** (1906), 1395.
615. H. M. Elsey. *J. Am. Chem. Soc.* **42** (1920), 2080.
616. D. Holde and S. Weill. *Brennstoff-Chem.* **4** (1923), 177 [*C. A.* **17**, 3771].
617. F. W. Atack and John Anderson. U. S. 1,430,277 (1922) [*C. A.* **16**, 3903].
618. M. T. Bogert and E. M. Abrahamson. *J. Am. Chem. Soc.* **44** (1922), 823.
619. Ger. 135,561 (1902); *Frd.* **VI**, 298; *Win.* **II**, 771.
620. Ger. 137,495 (1902); *Frd.* **VII**, 161; *Win.* **I**, 947.
621. Conrad Schraube. *Ber.* **8** (1875), 617.
622. Ger. 73,354 (1894); *Frd.* **III**, 954; *Win.* **I**, 1054.
623. Theodor Curtius and Gustav Ehrhart. *Ber.* **55B** (1922), 1562 [*C. A.* **16**, 3884].
624. Richard Möhlau and E. Fritzsche. *Ber.* **26** (1893), 1035.
625. Emilio Nölting and O. N. Witt. *Ber.* **17** (1884), 78.
626. Heinrich Wieland and Wilhelm Rheinheimer. *Ann.* **423** (1921), 16 [*C. A.* **15**, 2634].
627. K. G. MacKensie. *J. Ind. Eng. Chem.* **1** (1909), 360.
628. W. G. Wilcox. *J. Phys. Chem.* **14** (1910), 583 [*C. A.* **4**, 2226].
629. Bernardo Oddo. *Gazz. chim. ital.* **50** (1920) **II**, 272 [*C. A.* **15**, 2273].
630. Th. Zerewitinoff. *Z. anal. Chem.* **50** (1911), 683 [*C. A.* **6**, 203].
631. A. P. Tanberg. *J. Am. Chem. Soc.* **36** (1914), 335.
632. Th. Zerewitinoff. *Ber.* **47** (1914), 2417 [*C. A.* **9**, 75].
633. Th. Zerewitinoff and J. Ostromysslensky. *Ber.* **44** (1911), 2402 [*C. A.* **5**, 3814].
634. C. R. Downs. U. S. 1,290,124 (1919) [*C. A.* **13**, 731].
635. J. G. Heap *et al.* *J. Am. Chem. Soc.* **43** (1921), 1936.
636. W. M. Dehn. *J. Am. Chem. Soc.* **39** (1917), 1399.
637. Maurice Piettre. *Compt. rend.* **176** (1923), 1329 [*C. A.* **17**, 2624].
638. M. Cremer. *Z. Biol.* **36** (1898), 124 [*Zentr.* **1898 I**, 347].
639. K. Feist and H. Bestehorn. *Arch. Pharm.* **262** (1924), 296 [*C. A.* **18**, 3449].
640. D. G. Murdoch and W. L. Galbraith. Brit. 203,059 (1922) [*C. A.* **18**, 536].
641. Carl Neuberg. *Ber.* **32** (1899), 3384.
642. Robert Behrend. *Ann.* **353** (1907), 106; **377** (1910), 220 [*C. A.* **1**, 2234; **5**, 468].
643. A. W. Mangam and S. F. Acree. *J. Am. Chem. Soc.* **39** (1917), 967.
644. Roger Adams and H. Gilman. *J. Am. Chem. Soc.* **37** (1915), 2717.
645. A. Verley and Fr. Bölsing. *Ber.* **34** (1901), 3354.
646. M. Raffo and G. Rossi. *Gazz chim. ital.* **44** (1914) **I**, 104 [*C. A.* **8**, 2683].
647. Anna Mannessier. *Gazz. chim. ital.* **46** (1916) **I**, 233 [*C. A.* **10**, 2892].

648. Ger. 134,139 (1902); *Frd.* **VI**, 589; *Win.* **II**, 542.
649. Ger. 42,053 (1887); *Frd.* **I**, 305; *Win.* **I**, 941.
650. J. H. Walton and H. A. Lewis. *J. Am. Chem. Soc.* **38** (1916), 633.
651. Roland Scholl and Hans Berblinger. *Ber.* **36** (1903), 3429.
652. J. Otto. *Z. physiol. Chem.* **7** (1882–3), 57 [*Zentr.* **1883**, 553].
653. Ger. 83,046 (1895); *Frd.* **III**, 1011; *Win.* **II**, 466.
654. F. S. Hyde. *J. Ind. Eng. Chem.* **1** (1909), 377.
655. E. Noelting and Ch. Schwartz. *Ber.* **24** (1891), 1606.
656. Ira Remsen and S. R. McKee. *Am. Chem. J.* **18** (1896), 798 [*Zentr.* **1897 I**, 232].
657. *Oliën, Vetten en Oliezaden* **6** (1921), 329 [*C. A.* **16**, 1126].
658. John Marshall. *Am. J. Pharm.* **79** (1907), 315 [*C. A.* **1**, 2289].
659. C. Liebermann. *Ber.* **23** (1890), 142.
660. Johannes Wislicenus. *Ann.* **272** (1892), 19 [*Zentr.* **1892 II**, 965].
661. Ferd. Tiemann and Paul Krüger. *Ber.* **26** (1893), 2687.
662. K. v. Auwers and K. Hüttenes. *Ber.* **55B** (1922), 1114 [*C. A.* **16**, 3654].
663. Heinrich Wieland. *Ber.* **48** (1915), 1096 [*C. A.* **9**, 2538].
664. M. Gomberg. *J. Am. Chem. Soc.* **36** (1914), 1147.
665. M. Gomberg and C. S. Schoepfle. *J. Am. Chem. Soc.* **37** (1915), 2572.
666. F. M. Jaeger. *Proc. Acad. Sci. Amsterdam* **10** (1908) [2], 795 [*C. A.* **3**, 317].
667. Rob. Henriques. *Z. angew. Chem.* **1895**, 721 [*Zentr.* **1896 I**, 400].
668. H. W. Hillyer. *Trans. Wis. Acad. Sci.* **10** (1895), 367.
669. R. R. Read and Frederic Prisley. *J. Am. Chem. Soc.* **46** (1924), 1513.
670. M. D. Mann, Jr., and R. R. Williams. U. S. 1,365,043 (1921) [*C. A.* **15**, 944].
671. F. Weehuizen. *Rec. trav. chim.* **37** (1917), 266 [*C. A.* **13**, 708].
672. Brit. 183,419 (1921) [*C. A.* **17**, 212].
673. Fr. Heusler. *Ann.* **260** (1890), 228 [*Zentr.* **1890 II**, 1008].
674. R. L. Andreau. U. S. 1,381,782 (1921) [*C. A.* **15**, 3499].
675. L. H. Cone. U. S. 1,503,984 (1924) [*C. A.* **18**, 3193].
676. Mortimer Harvey and L. H. Baekeland. *J. Ind. Eng. Chem.* **13** (1921), 138.
677. Paul Landauer and Hugo Weil. *Ber.* **43** (1910), 201 [*C. A.* **4**, 1045].
678. Ernst Täuber and Richard Loewenherz. *Ber.* **24** (1891), 2598.
679. Ger. 61,711 (1892); *Win.* **II**, 507.
680. Arthur Lapworth *et al.* *J. Chem. Soc.* **111** (1917), 778 [*C. A.* **11**, 3023].
681. Sidney Young. Ref. 308, pp. 113, 149, 205.
682. Edward Kremers *et al.* *J. Am. Pharm. Assoc.* **7** (1918), 343; **9** (1920), 857, 860, 1042, 1153; **10** (1921), 26 [*C. A.* **12**, 2043; **15**, 730, 1492, 2338].
683. C. S. Leonard. *J. Am. Chem. Soc.* **43** (1921), 2621.
684. Edward Kremers. *Midland Druggist* **43** (1909), 55 [*C. A.* **4**, 2712].
685. H. Skellon. *India Rubber J.* **46** (1913), 251 [*C. A.* **7**, 3670].
686. C. S. Venable and C. D. Greene. *J. Ind. Eng. Chem.* **14** (1922), 319.
687. H. A. Endres. *India Rubber World* **68** (1923), 635 [*C. A.* **17**, 3627].
688. W. J. Kelly and K. B. Ayers. *Ind. Eng. Chem.* **16** (1924), 148.
689. G. Bruni. *Giorn. chim. ind. applicata* **3** (1921), 51 [*C. A.* **15**, 2018].
690. C. S. Venable and Tyler Fuwa. *J. Ind. Eng. Chem.* **14** (1922), 139.
691. C. Liebermann and A. Seyewetz. *Ber.* **24** (1891), 788.
692. C. Schwalbe. *Z. Farben Textil-Ind.* **3** (1904), 461 [*Zentr.* **1905 I**, 360].
693. A. Goldberg. *Z. angew. Chem.* **12** (1899), 75 [*Zentr.* **1899 I**, 544].
694. A. Haller and E. Michel. *Bull. soc. chim.* [3] **15** (1896), 1065 [*Zentr.* **1896 I**, 994].

695. K. Farnsteiner. *Z. Nahr. Genussm.* **2** (1899), 9 [*Zentr.* **1899 I**, 545].

696. P. W. Carleton. *J. Am. Chem. Soc.* **38** (1916), 1131.

697. Joseph Truhlar. *Ber.* **20** (1887), 669.

698. Roger Adams and H. Gilman. *J. Am. Chem. Soc.* **37** (1915), 2718.

699. C. Liebermann and Ludw. Limpach. *Ber.* **25** (1892), 927.

700. N. Kishner. *J. Russ. Phys.-Chem. Soc.* **23** (1891), 21 [*Ber.* **24** (1891), R559].

701. Ernst Wirth. Ger. 122,852 (1901); *Frd.* **VI**, 48; *Win.* **I**, 944.

702. L. Vignon and E. Evieux. *Bull. soc. chim.* [4] **3** (1908), 1012 [*C. A.* **3**, 736].

703. C. Liebermann. *Ber.* **26** (1893), 853.

704. Ger. 68,960 (1893); *Frd.* **IV**, 822; *Win.* **I**, 522; Ger. 81,264 (1895); *Frd.* **IV**, 253; *Win.* **II**, 201.

705. M. Heidelberger. *J. Biol. Chem.* **53** (1922), 34 [*C. A.* **16**, 3495].

706. M. L. Weiss. U. S. 1,422,506 (1922) [*C. A.* **16**, 3094].

707. Wilhelm Staedel. *Ann.* **283** (1894), 165 [*Zentr.* **1895 I**, 216].

708. M. Gomberg and F. W. Sullivan, Jr. *J. Am. Chem. Soc.* **44** (1922), 1814).

709. L. M. Dennis. U. S. 1,228,414 (1917); 1,332,203 (1920) [*C. A.* **11**, 2263; **14**, 1123].

710. L. Ruzicka and H. Trebler. *Helvetica Chim. Acta* **4** (1921), 676 [*C. A.* **16**, 87].

711. J. W. Brühl. *Ber.* **36** (1903), 668; **37** (1904), 749.

712. S. M. Malmgren. *Ber.* **36** (1903), 2609.

713. W. Tschelinzeff. *Ber.* **37** (1904), 4538.

714. Alex. McKenzie. *Brit. Assoc. Advancement Sci., Repts.* 1907, 293.

715. *C. A.* **18**, 1505; *Zentr.* **1923 IV**, 539.

716. C. A. Bischoff. *Ber.* **24** (1891), 1046.

717. J. W. Brühl. *Ber.* **24** (1891), 3378; Ger. 57,944 (1891); *Frd.* **III**, 23; *Win.* **I**, 427.

718. A. S. Wheeler. *J. Am. Chem. Soc.* **42** (1920), 1842.

719. A. S. Wheeler and I. W. Smithey. *J. Am. Chem. Soc.* **43** (1921), 2611.

720. Karol Dziewonski. *Ber.* **53**B (1920), 2181 [*C. A.* **15**, 1312].

721. Iwan Ostromysslensky. *J. prakt. Chem.* [2] **76** (1907), 268 [*C. A.* **2**, 656].

722. Ger. 56,563 (1890); *Frd.* **II**, 269; *Win.* **I**, 829.

723. Ger. 72,833 (1893); *Frd.* **III**, 427.

724. W. J. Hale and W. V. Hoyt. *J. Am. Chem. Soc.* **37** (1915), 2544.

725. H. Erdmann. Ger. 123,695 (1901); *Frd.* **VI**, 550; *Win.* **II**, 534.

726. L. A. Linton. *J. Am. Chem. Soc.* **16** (1894), 817.

727. Constantin Zwenger. *Ann.* **66** (1848), 7 [*Zentr.* **1848**, 569].

728. Emil Fischer and Helmuth Schiebler. *Ann.* **383** (1911), 359 [*C. A.* **5**, 3686].

729. Albert Henning. Brit. 152,550 (1919) [*C. A.* **15**, 737].

730. Albert Henning. Brit. 158,494 (1920) [*C. A.* **15**, 1954].

731. E. Beckmann. *Chem. Ztg.* **30** (1906), 484.

732. A. Hantzsch and O. K. Hofmann. *Ber.* **44** (1911), 1777 [*C. A.* **5**, 3258].

733. Charles Baskerville and W. A. Hamor. *J. Ind. Eng. Chem.* **4** (1912), 278.

734. Charles Baskerville and W. A. Hamor. *J. Ind. Eng. Chem.* **4** (1912), 499.

735. L. M. van den Berg. *C. A.* **13**, 1368; *Zentr.* **1919 II**, 798.

736. Richard Anschütz. *Ann.* **273** (1893), 77 [*Zentr.* **1893 I**, 153]; Ger. 70,614 (1893); *Frd.* **III**, 825; *Win.* **I**, 17.

737. Dorothy Hall. *J. Am. Chem. Soc.* **44** (1922), 1462.

738. C. J. Peddle and W. E. S. Turner. *J. Chem. Soc.* **103** (1913), 1202 [*C. A.* **7**, 3316].

739. Karl Freudenberg and Daniel Peters. *Ber.* **52**B (1919), 1465 [*C. A.* **14**, 1330].
740. Sven Odèn. *C. A.* **12**, 581.
741. Rudolph Gaze. *Arch. Pharm.* **228** (1890), 604 [see *Zentr.* **1890 I**, 590].
742. Ernst Schmidt. *Arch. Pharm.* **225** (1887), 145 [*Zentr.* **1887**, 388].
743. H. M. Gordin and C. G. Merrell. *Arch. Pharm.* **239** (1901), 636 [*Zentr.* **1901 II**, 1229].
744. P. Sisley. *Bull. soc. chim.* [4] **21** (1917), 155 [*C. A.* **12**, 7].
745. Clifford Richardson and C. N. Forrest. *J. Soc. Chem. Ind.* **24** (1905), 310.
746. C. K. Ingold and W. J. Powell. *J. Chem. Soc.* **119** (1921), 1227 [*C. A.* **15**, 3622].
747. Clive Newcomb. *Analyst* **49** (1924), 225 [*C. A.* **18**, 2858].
748. Otto Rammstedt. *Chem. Ztg.* **33** (1909), 93 [*C. A.* **3**, 1097].
749. *Chem. Ztg.* **31** (1907), 326 [*C. A.* **1**, 1778].
750. Charles Baskerville and H. S. Riederer. *J. Ind. Eng. Chem.* **4** (1912), 645.
751. P. Friedlander. *Monatsh.* **19** (1898), 636 [*Zentr.* **1899 I**, 610].
752. M. T. Bogert and W. F. Hand. *J. Am. Chem. Soc.* **24** (1902), 1032.
753. Joh. Pinnow and E. Muller. *Ber.* **28** (1895), 151.
754. J. P. Snyder. *J. Am. Pharm. Assoc.* **7** (1918), 966 [*C. A.* **13**, 499].
755. Courtney Conover and H. D. Gibbs. U. S. 1,301,388 (1919) [*C. A.* **13**, 1863].
756. W. Herz and W. Rathmann. *Chem. Ztg.* **36** (1912), 1417; **37** (1913), 621 [*C. A.* **7**, 1318, 3866]; *Z. Elektrochem.* **19** (1913), 887 [*C. A.* **8**, 1896].
B. M. Margosches. *Chem. Ztg.* **37** (1913), 509, 519 [*C. A.* **7**, 2545].
See also *Chem. Ztg.* **31** (1907), 1095; **32** (1908), 256, 528 [*C. A.* **2**, 717, 2314].
757. Alexander Wacker. *Chem. Ztg.* **45** (1921), 266 [*C. A.* **15**, 1851].
758. Sven Bodforss. *C. A.* **17**, 3157.
759. Karl Dangelmajer. *Chem. Ztg.* **42** (1918), 290 [*C. A.* **13**, 2958].
760. James Baddiley *et al.* U. S. 1,452,481 (1923) [*C. A.* **17**, 1969].
761. T. Tomiyama and K. Miyazaki. *C. A.* **16**, 1252.
762. C. S. Palmer and Roger Adams. *J. Am. Chem. Soc.* **44** (1922), 1365, 1370.
763. L. C. Daniels. U. S. 1,365,024 (1921) [*C. A.* **15**, 865].
764. F. S. Mortimer and R. V. Murphy. *Ind. Eng. Chem.* **15** (1923), 1141.
765. H. F. Lewis. U. S. 1,420,198 (1922) [*C. A.* **16**, 2867].
766. H. F. Lewis. U. S. 1,429,514 (1922) [*C. A.* **16**, 3903].
767. M. Gomberg and D. L. Tabern. *J. Ind. Eng. Chem.* **14** (1922), 1116.
768. J. B. Conant and A. W. Sloan. *J. Am. Chem. Soc.* **47** (1925), 577.
769. M. Gomberg and C. S. Schoepfle. *J. Am. Chem. Soc.* **39** (1917), 1655.
770. O. Lehmann. *Physik. Z.* **11** (1910), 47 [*C. A.* **4**, 1256].
771. Th. Sidot. *Compt. rend.* **69** (1869), 1305.
772. H. Arctowski. *Z. anorg. Chem.* **6** (1894), 257 [*Zentr.* **1894 II**, 17].
773. S. Cloëz. *Compt. rend.* **69** (1869), 1356 [*Zentr.* **1870**, 66].
774. E. C. McKelvy and D. H. Simpson. *J. Am. Chem. Soc.* **44** (1922), 108.
775. L. H. Friedburg and J. A. Mandel. *J. Am. Chem. Soc.* **12** (1890), 7.
776. H. Voss. *Chem. Ztg.* **45** (1921), 721 [*C. A.* **15**, 3415].
777. G. Wenzel. *Ber.* **33** (1900), 2041.
778. S. J. C. Olivier. *Rec. trav. chim.* **33** (1914), 129 [*C. A.* **8**, 3013].
779. P. J. Montagne. *Rec. trav. chim.* **40** (1921), 247 [*C. A.* **15**, 3476].
780. R. E. Wilson and E. W. Fuller. *J. Ind. Eng. Chem.* **14** (1922), 408.
781. S. J. Peachy. *J. Soc. Dyers Colourists* **30** (1914), 84 [*C. A.* **8**, 1673].
782. Max Mueller. *Chem. Met. Eng.* **23** (1920), 833 [*C. A.* **15**, 509].

783. E. Valenta. *Chem. Ztg.* **30** (1906), 266 [*Zentr.* **1906 I**, **1912**].
784. Ed. Graefe. *Chem. Umschau* **14** (1907), 112 [*C. A.* **1**, 1907].
785. H. M. Dawson *et al.* *J. Chem. Soc.* **93** (1908), 2063 [*C. A.* **3**, 740].
786. F. W. Atack and George Robertson. Brit. 173,805 (1920) [*C. A.* **16**, **1780**]; U. S. 1,401,125 (1921) [*C. A.* **16**, 934].
787. F. W. Atack and C. W. Soutar. Brit. 185,137 (1921) [*C. A.* **17**, 212].
788. A. Schönberg and F. Nedzati. *Ber.* **54**B (1921), 240 [*C. A.* **15**, 2090].
789. L. Vignon. *Bull. soc. chim.* [4] **3** (1908), 1030 [*C. A.* **3**, 422].
790. S. Gabriel. *Ber.* **19** (1886), 837.
791. C. Graebe and A. Philips. *Ber.* **24** (1891), 2298.
792. H. M. Roberts and C. R. Bury. *J. Chem. Soc.* **123** (1923), 2037 [*C. A.* **17**, 3826].
793. Paul Seidel. *Ber.* **23** (1890), 184.
794. R. H. McKee and F. A. Strauss. *Chem. Met. Eng.* **24** (1921), 699 [*C. A.* **15**, 1703].
F. A. Strauss. U. S. 1,367,898 (1921) [*C. A.* **15**, 1029].
795. F. A. Strauss. U. S. 1,367,898 (1921) [*C. A.* **15**, 1029].
796. L. M. Dennis and F. E. Hance. *J. Am. Chem. Soc.* **47** (1925), 371.
797. A. Windaus and F. Klänhardt. *Ber.* **54**B (1921), 584 [*C. A.* **15**, 2628].
798. W. L. Jennings and W. B. Scott. *J. Am. Chem. Soc.* **41** (1919), 1244.
799. J. G. Spenzer. *J. Am. Chem. Soc.* **17** (1895), 8.
800. A. J. Boyd *et al.* *J. Chem. Soc.* **117** (1920), 1388 [*C. A.* **15**, 511].
801. John Read and Eric Hurst. *J. Chem. Soc.* **121** (1922), 2553 [*C. A.* **17**, **559**].
802. Carl Wolff. *Ber.* **25** (1892), 3031.
803. Guido Banse. *Ber.* **27** (1894), 2165.
804. Brit. 200,511 (1923) [*C. A.* **18**, 274].
805. H. J. M. Creighton. *Proc. Trans. Nova Scotian Inst. Sci.* **15** (1918–19), 57 [*C. A.* **16**, 2993].
806. J. Berdez and M. Nencki. *Arch. exptl. Path. Pharmakol.* **20** (1886), 350 [*Zentr.* **1886**, 889].
807. Br. Pawlewski. *Ber.* **23** (1890), 328.
808. Robert Fricke. *Z. Elektrochem.* **28** (1922), 244 [*C. A.* **16**, 3568].
809. Louis Dede. *Z. Elektrochem.* **28** (1922), 364 [*C. A.* **16**, 3779].
810. Robert Fricke. *Z. Elektrochem.* **28** (1922), 365 [*C. A.* **16**, 3779].
811. Robert Fricke. *Kolloid-Z.* **31** (1923), 80 [*Zentr.* **1923** I, 1609].
812. Robert Fricke. *Z. Elektrochem.* **29** (1923), 44 [*C. A.* **17**, 1184].
813. S. W. Young. *J. Am. Chem. Soc.* **33** (1911), 148.
814. S. W. Young and W. J. Van Sicklen. *J. Am. Chem. Soc.* **35** (1913), 1075.
815. S. W. Young and R. J. Cross. *J. Am. Chem. Soc.* **33** (1911), 1375.
816. W. A. Noyes and R. S. Potter. *J. Am. Chem. Soc.* **37** (1915), 200.
817. M. Nencki. *Arch. exptl. Path. Pharmakol.* **20** (1886), 338 [*Zentr.* **1886**, **937**].
818. A. Herzfeld. *Ber.* **12** (1879), 2120.
819. W. J. Karslake and P. A. Bond. *J. Am. Chem. Soc.* **31** (1909), 410.
820. S. W. Young and W. E. Burke. *J. Am. Chem. Soc.* **29** (1907), 329.
S. W. Young. *J. Am. Chem. Soc.* **33** (1911), 148.
821. A. Williamson. *Proc. Royal Soc. (London)* **7** (1854), 18.
822. T. L. Davis. *J. Am. Chem. Soc.* **41** (1919), 1138.
823. A. H. Gotthelf. *J. Am. Chem. Soc.* **23** (1901), 627.
824. D. C. Wilson. *Pharm. J.* **110** (1923), 363 [*C. A.* **17**, 2171].

825. D. B. Dott. *Pharm. J.* **111** (1923), 661 [*C. A.* **18**, 1413].
826. E. P. Kohler and L. I. Smith. *J. Am. Chem. Soc.* **44** (1922), 629.
827. A. G. Green. *Ber.* **26** (1893), 2778.
828. M. Gomberg and L. H. Cone. *Ber.* **39** (1906), 2961.
829. J. M. Bell *et al.* *J. Ind. Eng. Chem.* **13** (1921), 59.
830. J. G. Spenzer. *J. Am. Chem. Soc.* **17** (1895), 21.
831. H. Thoms. *Ber.* **41** (1908), 2759 [*C. A.* **2**, 3356].
832. J. d'Ans and W. Frey. *Ber.* **45** (1912), 1849 [*C. A.* **6**, 2737].
833. A. J. Hill and E. B. Kelsey. *J. Am. Chem. Soc.* **44** (1922), 2359.
834. J. A. Middendorp. *Rec. trav. chim.* **38** (1919), 6 [*C. A.* **13**, 2345].
835. L. Scholvein. Fr. 335,013 (1903); *Win.* **III**, 433.
836. Ger. 111,359 (1900); *Frd.* **VI**, 46; *Win.* **I**, 943.
837. D. F. Gould. U. S. 1,431,394 (1922) [*C. A.* **16**, 4215].
838. Ed. Bourgeois and J. Dambmann. *Ber.* **26** (1893), 2857.
839. Dan Tyrer. *J. Chem. Soc.* **97** (1910), 1778 [*C. A.* **4**, 3159].
840. Philip Blackman. *J. Phys. Chem.* **13** (1909), 436 [*C. A.* **3**, 2400].
841. Michael Heidelberger and W. A. Jacobs. *J. Am. Chem. Soc.* **41** (1919), 2138.
842. S. Genelin. *Z. physik. chem. Unterricht* **33** (1920), 147 [*C. A.* **14**, 3559].
843. Edmund Speyer and Sigurd Siebert. *Ber.* **54B** (1921), 1528 [*C. A.* **15**, 3975].
844. Alfred Ahlqvist. *J. prakt. Chem.* [2] **99** (1919), 52 [*C. A.* **14**, 47].
845. C. Ulpiani. *Gazz. chim. ital.* **46** (1916) I, 18 [*C. A.* **10**, 2879].
846. J. B. Tingle and S. J. Bates. *J. Am. Chem. Soc.* **32** (1910), 1323.
847. C. F. Mabery. *Ind. Eng. Chem.* **15** (1923), 1233.
848. A. S. Wheeler and R. W. Bost. *J. Am. Chem. Soc.* **46** (1924), 2814.
849. W. G. Christiansen. *J. Am. Chem. Soc.* **45** (1923), 2193.
850. K. Charitschoff. C. Engler and H. v. Höfer "Das Erdöl" (S. Hirzel, Leipzig, 1913), Vol. **I**, p. 510. See also *C. A.* **2**, 1042.
851. C. Engler. Ref. 850, p. 43.
852. J. Houben. *J. prakt. Chem.* [2] **105** (1922), 20 [*C. A.* **17**, 1622.]
853. E. O. Ellingson. *J. Am. Chem. Soc.* **36** (1914), 325.
854. H. A. Torrey and C. M. Brewster. *J. Am. Chem. Soc.* **35** (1913), 432.
855. Arthur Michael. *Ann.* **391** (1912), 238 [*C. A.* **6**, 3415].
856. M. S. Kharasch and Lyman Chalkley, Jr. *J. Am. Chem. Soc.* **46** (1924), 1219.
857. C. Graebe and O. Schultess. *Ann.* **263** (1891), 8 [*Zentr.* **1891 I**, 1058].
858. M. Gomberg and E. C. Britton. *J. Am. Chem. Soc.* **43** (1921), 1946.
859. Heinrich Bayer. *Z. physiol. Chem.* **3** (1879), 303.
860. A. Partheil. *Ber.* **24** (1891), 636.
861. W. D. Bonner. *J. Phys. Chem.* **14** (1910), 738 [*C. A.* **5**, 817].
862. G. Hufner. *J. prakt. Chem.* [2] **10** (1874), 267 [*Zentr.* **1874**, 723].
863. Emil Bosetti. *Arch. Pharm.* **221** (1883), 84 [*Zentr.* **1883**, 435].
864. Richard Fischer. *J. Am. Chem. Soc.* **14** (1892), 229.
865. G. S. Jamieson and E. T. Wherry. *J. Am. Chem. Soc.* **42** (1920), 138.
866. A. Seidenberg. *J. Ind. Eng. Chem.* **9** (1917), 855.
867. A. Rümpler. *Ber.* **33** (1900), 3474.
868. P. P. von Weimarn. *Kolloid-Z.* **32** (1923), 145 [*C. A.* **17**, 3438].
869. H. von Euler and E. Löwenhamm. *Z. Elektrochem.* **22** (1916), 199, 254 [*C. A.* **10**, 3021; **11**, 915].
870. J. C. Philip. *J. Chem. Soc.* **87** (1905), 987.
871. J. C. Philip and F. B. Garner. *J. Chem. Soc.* **95** (1909), 1466 [*C. A.* **4**, 137].

872. P. Pfeiffer and J. Würgler. *Z. physiol. Chem.* **97** (1916), 128 [*C. A.* **11**, 334].
873. Hans Euler. *Z. physiol. Chem.* **97** (1916), 291 [*C. A.* **11**, 334].
874. Harald Lundén. *Z. physik. Chem.* **54** (1905), 564 [*Zentr.* **1906 I**, 1014].
875. E. G. Thorin. *Z. physik. Chem.* **89** (1915), 688 [*C. A.* **9**, 2342].
876. H. von Euler. *Z. Elektrochem.* **23** (1917), 192 [*C. A.* **12**, 557].
877. H. von Euler. *Physik. Z.* **18** (1917), 113 [*C. A.* **12**, 557].
878. Olaf Svanberg. *C. A.* **12**, 557; *Zentr.* **1918 II**, 1011.
879. Hans Euler and Karin Rudberg. *C. A.* **19**, 597.
880. Ebbe Linde. *C. A.* **12**, 558; *Zentr.* **1918 II**, 1022.
881. A. C. D. Rivett and E. I. Rosenblum. *Trans. Faraday Soc.* **9** (1913), 297 [*C. A.* **8**, 2292].
882. E. Bourgoin. *Bull. soc. chim.* [2] **29** (1878), 247 [*Zentr.* **1878**, 243].
883. W. Herz. *Z. anorg. Chem.* **65** (1909), 341 [*C. A.* **4**, 1417].
884. Fr. Hoffmann and K. Langbeck. *Z. physik. Chem.* **51** (1905), 385 [*Zentr.* **1905 I**, 1292].
885. T. N. Whitelaw. *J. Soc. Chem. Ind.* **5** (1886), 90.
886. W. T. Cooke. *J. Soc. Chem. Ind.* **40** (1921), 56T, 239T [*C. A.* **15**, 1699; **16**, 92].
887. P. C. L. Thorne. *J. Chem. Soc.* **119** (1921), 262 [*C. A.* **15**, 1842].
888. H. W. Hochstetter. *J. Am. Chem. Soc.* **20** (1898), 549.
889. Ludwig Gattermann. "The Practical Methods of Organic Chemistry," translated by W. B. Schober and V. S. Babasinian (Macmillan, New York, 1916), p. 280.
890. U. S. P. IX (1916), p. 592.
891. G. D. Beal and T. S. Hamilton. *J. Am. Pharm. Assoc.* **9** (1920), 11 [*C. A.* **14**, 1004].
892. J. W. T. Knox and A. B. Prescott. *J. Am. Chem. Soc.* **20** (1898), 45.
893. H. C. Sherman and A. P. Tanberg. *J. Am. Chem. Soc.* **38** (1916), 1641.
894. M. Gomberg. *J. Am. Chem. Soc.* **41** (1919), 1426.
895. Adolf Baeyer. *Ber.* **10** (1877), 1079.
896. Adolf Baeyer. *Ber.* **12** (1879), 1317.
897. Arthur Weinberg. *Ber.* **20** (1887), 3174.
898. H. A. Lubs. *J. Ind. Eng. Chem.* **11** (1919), 456.
899. A. Hantzsch and Robert Robison. *Ber.* **43** (1910), 93 [*C. A.* **4**, 925].
900. M. Heidelberger and W. A. Jacobs. *J. Am. Chem. Soc.* **41** (1919), 2138.
901. W. Kühne and R. H. Chittenden. *Z. Biol.* **22** (1886), 424 [*Zentr.* **1887**, 1045].
902. Ger. 70,281 (1893); *Win.* **I**, 1224.
903. E. T. Reichert. *Am. J. Physiol.* **9** (1903), 97 [*Zentr.* **1903 I**, 1146].
904. Robert Otto. *Ber.* **27** (1894), 2131.
905. Joh. Pinnow and G. Pistor. *Ber.* **26** (1893), 1314.
906. Heinrich Wienhaus. *Ber.* **53**B (1920), 1659 [*C. A.* **15**, 844].
907. P. A. Kober. *J. Am. Chem. Soc.* **41** (1919), 444.
908. Carl Weitenkampf. Ger. 57,393 (1890), 69,884 (1893).

INDEX OF AUTHORS

Abderhalden, Emil, *see* Diels, Otto
Abe, Ryuji, 92
Abrahamson, E. M., *see* Bogert, M. T.
Acree, S. F., *see* Mangam, A. W., *and* Robertson, H. C.
Adams, C. C., *see* Grob, A. R.
Adams, Roger, and Gilman, H., 111, 124
  and Marvel, C. S., 51
  see also Palmer, C. S.
Adkins, Homer, 64
  see also Oyster, Leone
de Aguiar, A. A., and Bayer, Alex, 97
Ahlqvist, Alfred, 152
Allison, V. C., *see* Jones, G. W.
Anders, G., *see* Knoch, M., *et al.*
Anderson, John, *see* Atack, F. W.
Andreau, R. L., 118
Andrews, L. W., 57, 58, 60, 64, 69, 71, 73
d'Ans, J., and Frey, W., 150
Anschütz, Richard, 131
Antony, U., and Magri, G., 37
Antusch, A. C., *see* Holleman, A. F.
Archibald, E. H., 36
  and McIntosh, D., 36
Arctowski, H., 136
Arnall, Francis, 11
Aschan, Ossian, 95
Atack, F. W., 98
  and Anderson, John, 106, 118, 128
  and Robertson, George, 139
  and Soutar, C. W.
Auwers, K. v., and Hüttenes, K., 116
Ayers, K. B., *see* Kelly, W. J.

Backhaus, A. A., 67
Baddiley, James, *et al*, 135
Baekeland, L. H., *see* Harvey, Mortimer
Baeyer, Adolf, 28, 165
Bailey, G. C., *see* Johnson, T. B.
Bailey, J. R., and Pritchett, R. H., 93
  et al, 93
Bamberger, Curt, *see* Dimroth, Otto
Bamberger, Max, and Nussbaum, Josef, 25
Bancroft, W. D., 12
Banse, Guido, 141
Bartels, A., *see* Jannasch, P.
Barth, L., *see* Hlasiwetz, H.
Bartow, Edward, and McFarland, D. F., 32
Baskerville, Charles, and Cohen, P. W., 100
  and Hamor, W. A., 82, 83, 85, 130
  and Riederer, H. S., 133
Bateman, W. G., and Conrad, D. B., 9
Bates, S. J., *see* Tingle, J. B.
Battegay, M., and Hugel, G., 29
Bayer, Alex, *see* de Aguiar, A. A.
Bayer, Heinrich, 155
Beaber, N. J., *see* Gilman, Henry
Beal, G. D., and Hamilton, T. S., 77, 163
Beckmann, E., 130
Beggs, S. A., *see* Jackson, C. L.
Behr, Arno, 19
Behrend, Robert, 110
Bekaert, A., *see* von Hemptinne, A.
Bell, J. M., *et al*, 149
Benedict, S. R., 16
Berblinger, Hans, *see* Scholl, Roland
Berdez, J., and Nencki, M., 143
Beringer, Emil, 105
Berkheiser, E. J., *see* McKee, R. H.
Bernthsen, August, 98
Berthelot, M., 88
  and St. Gilles, L. Péan de, 59
Bestehorn, H., *see* Feist, K.
Biedermann, H., 49
Bigelow, C. A., *see* Wollenberg, H. L.
Bigelow, L. A., 31
Bigelow, S. L., 4
Biltz, Heinrich, 47
Bischoff, C. A., 126
Bishop, E. R., *et al*, 46
Bishop, J. E., *see* Kraus, C. A.

Bissett, C. C., *see* Turner, W. E. S.
Bjerrum, Niels, and Zechmeister, Lászlô, 62
Blackman, Philip, 152
Blom, A. V., 30
Bodforss, Sven, 135
Boessneck, P., and Knoefler, O., 99
Bogert, M. T., and Abrahamson, E. M., 106
  and Hand, W. F., 6, 92, 134
  and Hoffman, Alfred, 88
  and Mandelbaum, M. R., 30, 31
Bölsing, Fr., *see* Verley, A.
Bolton, E. K., *see* Willstätter, R.
Bond, P. A., *see* Karslake, W. J.
Bosetti, Emil, 156
Bost, R. W., *see* Wheeler, A. S.
Boswell, M. C., and Corman, H. E., 95
Bourgeois, Ed., and Dambmann, J., 151
Bourgom, A., 39, 90
Bousfield, W. R., and Lowry, T. M., 91
Boyd, A. J., *et al*, 141
Bradfield, A. E., *see* Orton, K. J. P.
Brady, O. L., and Williams, P. N., 29
Brass, W., *see* Wallach, O.
Bredig, G., and Fraenkel, W., 69
Brègeat, J. H., 99
Brewster, C. M., *see* Torrey, H. A.
Brewster, R. Q., *see* Dains, F. B.
Britton, E. C., *see* Gomberg, M.
Brown, T. F., 11
Brownstein, H. J., *see* Hurd, C. D.
Brühl, J. W., 11, 89, 101, 126
Brunel, R. F., *et al*, 55, 58, 59, 61, 63, 73
Bruni, G., 121
Brunner, C., *see* Calloud
de Bruyn, Lobry, 19, 40, 41
Büchner, E. H., 37
Büchner, Eduard, and Witter, H., 18
Burke, W. E., *see* Young, S. W.
Burns, R. M., *see* Curtis, H. A.
Burrell, G. A., *et al*, 13
Bury, C. R., *see* Roberts, H. M.

Cable, D. E., *see* McKee, R. H.
Cain, J. C., and Thorpe, J. F., 26
Calloud and Brunner, C., 19
Calvert, H. T., 26
Calvert, R. P., *see* Schlesinger, H. I.
Carleton, P. W., 11, 86, 123
Carlton, C. A., 73
Carnelly, Thomas, and Thomson, Andrew, 4
Carrara, G., 11
Caspari, Chas., Jr., 52
Castille, A., and Henri, Victor, 72, 116
Cattini, E., *see* Cusmano, G.
Centnerszwer, M., 42
  see also Walden, P.
Chablay, E., 33
Chalkley, Lyman, Jr., *see* Kharasch, M. S.
Charitschoff, K., 153
Chavanne, G., 67
Chittenden, R. H., and Osborne, T. B., 7
  see also Kühne, W.
Christiansen, W. G., 153
Claisen, L., 63
Clancy, J. C., 33, 34
Clark, J. M., 16
Clarke, Latham, and Jones, W. N., 22
Clifford, C. W., 22, 33
Cloëz, S., 136
Clough, W. W., and Johns, C. O., 64, 130
Clover, A. M., 83
Cohen, J. B., 4
Cohen, Lillian, *see* Frankforter, G. B.
Cohen, P. W., *see* Baskerville, Charles
Cohn, Rudolf, 20
Conant, J. B., and Sloan, A. W., 136
Cone, L. H., 118
  see also Gomberg, M.
Conover, Courtney, and Gibbs, H. D., 134
Conrad, D. B., *see* Bateman, W. G.
Cook, A. N., and Haines, A. L., 59, 65
Cooke, W. T., 162
Coolidge, A. S., *see* Forbes, G. S.
Corman, H. E., *see* Boswell, M. C.
Crafts, J. M., *see* Friedel, C.
Creighton, H. J. M., 142
Cremer, M., 109
Crismer, L., 58, 59, 60, 62, 69, 73
Cross, R. J., *see* Young, S. W.
Cunlasse, *see* Girard
Curme, G. O., Jr., and Reid, E. W., 74
  and Young, C. O., 78
Curtis, H. A., and Burns, R. M., 44

Curtius, Theodor, and Ehrhart, Gustav, 107, 127
Cusmano, G., and Cattini, E., 87

Dains, F. B., and Brewster, R. Q., 33
  et al, 33
Dakin, H. D., 75
Dale, J. K., *see* Hudson, C. S.
Dambmann, J., *see* Bourgeois, Ed.
Dangelmajer, Karl, 135
Daniels, E. A., *see* Frankforter, G. B.
Daniels, L. C., 135
Danner, P. S., and Hildebrand, J. H., 57, 71
Darrah, J. E., and MacArthur, C. G., 88
Datta, Rasik Lal, and Gupto, S. Das, 21
Davis, T. L., 148
Dawson, H. M., *et al*, 138
Dawson, W. H., 98
Deane, Harold, and Edmonton, W. E., 6
Dede, Louis, 144
Dehn, W. M., 4, 7, 109
  see also Pucher, Geo.
Delachenal, *see* Vincent, C.
Deming, H. G., 23
Dennis, L. M., 126
  and Hance, F. M., 140
Descudé, Marcel, 88
Diels, Otto, and Abderhalden, Emil, 105
Dietze, Paul, 24
Dimroth, Otto, 11
  and Bamberger, Curt, 7
  see also Thiele, Johannes
Dort, R. G., *see* Roulleux, M.
Dott, D. B., 148
Dover, M. V., *see* Marden, J. W.
Downs, C. R., 109
Dox, A. W., and Yoder, Lester, 28, 51
Dreyfus, Henry, 97
Drummond, A. A., 99
Dubosc, André, 96, 101
Duclaux, J., and Lanzenberg, A., 103
  see also Lanzenberg, A.
Dumas, H. N., *see* Emerson, W. H.
Dumas, J., and Peligot, E., 40
Dunbrook, R. F., *see* Lowy, Alexander
Dunlap, F. L., 12, 71
Durand, J., 83
Dziewonski, Karol, 127
Eckenroth, H., 99
Edeleanu, L., 35
Edmonton, W. E., *see* Deane, Harold
Ehrhart, Gustav, *see* Curtius, Theodor
Eidmann, Wilhelm, 39
Ellingson, E. O., 154
Elsey, H. M., 106
Emerson, W. H., and Dumas, H. N., 46
Endres, H. A., 121
Engler, C., 153
Erbe, Rudolf, *see* Wislicenus, Wilhelm
Erdmann, Ernst, 104
Erdmann, Hugo, 79, 128
Erdmann, J., *see* Ulsar, L. von
Erhart, *see* Remy
Etti, C., 100
Euler, Hans von, 160
  and Löwenhamm, E., 158
  and Rudberg, Karin, 160
  and Svanberg, Olaf, 160
Evans, Thos., and Fetsch, W. C., 64
Evieux, E., *see* Vignon, L.
Ewan, Thos., and Young, J. G., 27

Farnsteiner, K., 123
Feist, K., 85
  and Bestehorn, H., 110
Fetsch, W. C., *see* Evans, Thos.
Fichter, Fr., and Grisard, Gustav, 29
  and Jaeck, Wolfgang, 29
Finnemore, Horace, *see* Wade, John
Fischer, Emil, 30
  and Schiebler, Helmuth, 130
  and Schmidmer, Eduard, 20
Fischer, Franz, and Jaeger, Albert, 22
Fischer, Richard, 156
Fischer, W. M., 52
Flaherty, E. M., 85
Flemming, H., 81
Fleysher, M. H., *see* Harned, H. S.
Forbes, G. S., and Coolidge, A. S., 22, 86
de Forcrand, 43
Forrest, C. N., *see* Richardson, Clifford
Fortey, E. C., *see* Young, Sidney
Fraenkel, W., *see* Bredig, G.
Frankforter, G. B., 54, 65
  and Cohen, Lillian, 103
  and Daniels, E. A., 85
  and Frary, F. C., 53, 58

Franklin, E. C., 32
  and Kraus, C. A., 32
  and Stafford, O. F., 33
Frary, F. C., *see* Frankforter, G. B.
Freudenberg, Karl, and Peters, Daniel, 131
Frey, W., *see* d'Ans, J.
Fricke, Robert, 144
Friedburg, L. H., 81
  and Mandel, J. A., 10, 136
Friedel, C., and Crafts, J. M., 63
Friedlander, P., 134
Fritzsche, E., *see* Möhlau, Richard
Froehlke, A. W., *see* Sherrard, E. C.
Fühner, H., 50, 162
Fuller, E. W., *see* Wilson, R. E.
Fuller, H. C., 74, 78
Fuwa, Tyler, *see* Venable, C. S.

Gabriel, S., 139
  and Leupold, Ernst, 101
Galbraith, W. L., *see* Murdoch, D. G.
Gallotti, G., and Giampalmo, G., 7
Garner, F. B., *see* Philip, J. C.
Garner, J. B., *et al*, 95
Gastalde, C., 92
Gattermann, Ludwig, 163
  and Ritschke, A., 96
Gaze, Rudolph, 132
Genelin, S., 152
Gerardin, A., 43
Germann, A. F. O., 98
Giampalmo, G., *see* Gallotti, G.
Gibbs, H. D., 106
  see also Conover, Courtney
Gilman, Henry, and Beaber, N. J., 85
  see also Adams, Roger
Girard and Cuniasse, 71
Gnehm, R., and Kaufler, F., 90
Godfrin, 79
Goebel, W. F., *see* Noyes, W. A.
Goldberg, A., 123
Goldschmidt, Heinrich, 61, 62, 68, 69
  and Sunde, Einar, 60
  and Thuesen, Arthur, 61
Gomberg, M., 104, 116, 164
  and Britton, E. C., 155
  and Cone, L. H., 149
  and Schoepfle, C. S., 117, 136
Gomberg, M., and Sullivan, F.W., Jr., 126
  and Tabern, D. L., 136
Gordin, H. M., and Merrell, C. G., 132
Gore, G., 32, 37
Gotthelf, A. H., 148
Göttig, Christian, 52
Gould, D. F., 151
Graebe, C., and Philips, A., 139
  and Schultess, O., 155
Graefe, Ed., 138
Grant, D. H., and Johns, C. O., 74
Green, A. G., 26, 81, 148
Greene, C. D., *see* Venable, C. S.
Greer, W. N., *see* Kraus, C. A.
Griffin, E. G., and Nelson, J. M., 94
Grisard, Gustav, *see* Fichter, Fr.
Grob, A. R., and Adams, C. C., 34
Grosschuff, E., 22
Groves, C. E., *see* Stenhouse, John
Guareschi, J., 10
Guérin, G., 85
Guinot, Henri, 67
Gupto, S. Das, *see* Datta, R. L.
Gyr, Joseph, 58, 61, 68

Haines, A. L., *see* Cook, A. N.
Hale, W. J., and Hoyt, W. V., 128
Hall, Dorothy, 131
Hall, R. A., 48
Haller, A., and Michel, E., 123
Hamilton, C. S., *see* Lewis, W. L.
Hamilton, T. S., *see* Beal, G. D.
Hammick, D. L., and Locket, G. H., 77
Hammond, J. A. S., 52, 84
Hamor, W. A., *see* Baskerville, Charles
Hance, F. M., *see* Dennis, L. H.
Hand, W. F., *see* Bogert, M. T.
Hantzsch, A., and Herrmann, F., 20
  and Hofmann, O. K., 130
  and Robison, Robert, 165
Harding, T. S., 95
Harned, H. S., and Fleysher, M. H., 58
Harris, J. E. G., and Pope, W. J., 27
Hartridge, H., 77
Harvey, Mortimer, and Baekeland, L. H., 119
Harvey, Newton, 21
Hatcher, W. H., *see* Maass, O.
Haussermann, J., *see* Wedekind, E.

Hawkins, A. J., 11
Haworth, Edw., and Perkin, W. H., Jr., 15
Hayduck, M., 9
Heap, J. G., *et al*, 109
Heidelberger, M., 125
  and Jacobs, W. A., 74, 152, 165
  see also Jacobs, W. A.
Heine, K., 28
von Hemptinne, A., and Bekaert, A., 11
Henning, Albert, 130
Henri, Victor, *see* Castille, A.
Henriques, Rob., 117
Henschel, Willibald, 99
Herrmann, F., 20
  see also Hantzsch, A.
Herz, W., 22, 161
  and Knoch, M., 44, 80
  and Kuhn, F., 41
  et al, 44
Herzfeld, A., 146
Herzog, J., 85
Hess, J. H., 53
Hesse, O., 19, 47
Heuser, Herman, 72
Heusler, Fr., 118
Heuter, R., 24
von Heyden, F., 24
Heyl, F. W., 97
Hildebrand, J. H., 4, 14
  see also Danner, P. S.
Hill, A. E., 39
Hill, A. J., and Kelsey, E. B., 150
  see also Johnson, T. B.
Hillyer, H. W., 117
Hirsch, R., 99
Hitch, E. F., *see* Orndorff, W. R.
Hlasiwetz, H., and Barth, L., 20
Hochstetter, H. W., 162
Hoffman, Alfred, *see* Bogert, M. T.
Hoffmann, Fr., and Langbeck, K., 161
Hoffmeister, Franz, 49
Hoffmeister, W., 99
Hofmann, Joseph, *see* Lecher, Hans
Hofmann, O. K., see Hantzsch, A
Holde, D., and Weill, S., 106
Holland, E. B., 46
Holleman, A. F., and Antusch, A. C., 47
Holm, G. E., *see* Renshaw, R. R.
Holm, K., 78, 80
Holmes, A. A., *see* McKee, R. H.
Houben, J., 153
Hoyt, W. V., *see* Hale, W. J.
Hübner, R., *see* Walther, R. von
Hudson, C. S., and Dale, J. K., 94
  and Sawyer, H. L., 94
Hufner, G., 156
Hugel, G., *see* Battegay, M.
Hugounenq, L., 90
Hunn, E. B., 6
Hunt, B. A., 48
Hurd, C. D., and Brownstein, H. J., 75
Hurst, Eric, *see* Read, John
Hüttenes, K., *see* Auwers, K. v.
Hyde, F. S., 114

Ingold, C. K., and Powell, W. J., 133
van Itallie, L., and van der Zande, J. E., 85

Jackson, C. L., and Beggs, S. A., 46
  and Lamar, W. R., 28
  and Robinson, W. S., 16
Jacobs, W. A., and Heidelberger, Michael, 105
  see also Heidelberger, M.
Jacobsohn, Felix, 4, 38
Jaeck, Wolfgang, *see* Fichter, Fr.
Jaeger, Albert, *see* Fischer, Franz
Jaeger, F. M., 117
Jamieson, G. S., and Wherry, E. T., 156
Jannasch, P., and Bartels, A., 13, 88
  and Rathjen, A., 88
Jaquet, Daniel, *see* Willstätter, R.
Jennings, W. L., and Scott, W. B., 140
Johns, C. O., *see* Clough, W. W., *and* Grant, D. H.
Johnson, T. B., and Bailey, G. C., 92
  and Hill, A. J., 30
  see also Pucher, G. W.
Johnston, John, 58, 59
Jones, D. C., *see* Orton, K. J. P.
Jones, G. W., and Allison, V. C., 1
Jones, W. N., *see* Clarke, Latham
Just, Gerhard, 5

Kailan, Anton, 56, 57, 62, 69
Kane, Robert, 53
Karslake, W. J., and Bond, P. A., 146

Kaufler, F., *see* Gnehm, R.
Kaufmann, Ludwig, *see* Wislicenus, Hans
Kebler, L. F., 52
Kelly, W. J., and Ayers, K. B., 121
Kelsey, E. B., *see* Hill, A. J.
Kennedy, J. J., *see* Orndorff, W. R.
Keyes, F. G., and Winninghoff, W. J., 62
Kharasch, M. S., and Chalkley, Lyman, Jr., 103, 155
Kiliani, H., 48
Kirby, William, 28
Kishner, N., 124
Klänhardt, F., *see* Windaus, A.
Klason, Peter, and Norlin, Evert, 61
Klepl, A., 43
Klever, 78
Klingemann, F., and Laycock, W. F., 77
Knecht, Edmund, and Muller, E. F., 54
Knoevenagel, Emil, 45
  and Weissgerber, R., 101
Knoch, M., *see* Herz, W., *et al*
Knoefler, O., *see* Boessneck, P.
Knorr, Ludwig, *et al*, 89
Knox, J. W. T., and Prescott, A. B., 101, 163
Knox, Jos., and Will, H. R., 27
Kober, P. A., 166
Kochmann, E. L., *see* Underwood, H. W., Jr.
Koehler, 101
Kohler, E. P., and Smith, L. I., 148
Kokatnur, V. R., 1
Kolbe, H., and Lautermann, E., 20
Kolthoff, I. M., 70
Konek, Fr. v., 59, 64
Kraus, C. A., and Bishop, J. E., 62
  and Greer, W. N., 33
  and White, G. F., 33
  see also Franklin, E. C.
Kremers, Edward, and Sherk, D. C. L., 120
Krieble, V. K., and Seyer, W. F., 35
Krug, W. H., and McElroy, K. P., 39
Krüger, Paul, *see* Tiemann, Ferd.
Kuhn, F., *see* Herz, W., *et al*
Kühne, W., and Chittenden, R. H., 166
Kulkarni, D. A., *see* Varma, P. S.
Küster, W., 76
Kyrides, L. P., 9
Laar, Conrad, 30
Lamar, W. R., *see* Jackson, C. L.
Lammert, O. M., *see* Morgan, J. L. R.
Landau, B., 7
Landauer, Paul, and Weil, Hugo, 119
Langbeck, K., *see* Hoffmann, Fr.
Lanzenberg, A., and Duclaux, J., 72
  see also Duclaux, J.
Lapworth, Arthur, and Partington, J. R., 60
  et al, 119
Lassar-Cohn, 17, 19, 46, 50, 83, 85, 89, 166
von Laszczynski, St., 38
Latschinoff, P., 17, 75
Lautemann, E., *see* Kolbe, H.
Laycock, W. F., *see* Klingemann, F.
LeBel, J. A., 66
Lebo, R. B., 53, 76
Lecher, Hans, and Hofmann, Joseph, 75
Lehmann, O., 136
Lenher, Victor, 37
Lenz, W., 30
Leonard, C. S., 120
Leupold, Ernst, *see* Gabriel, S.
Lewis, H. A., *see* Walton, J. H.
Lewis, H. F., 135
Lewis, W. L., and Hamilton, C. S., 93
Lichtenstadt, Leo, *see* Semper, Leopold
Liebermann, C., 116, 125
  and Limpach, Ludw., 124
  and Seyewitz, A., 122
Limpach, Ludw., *see* Liebermann, C.
Linde, Ebbe, 160
Lindemann, Thv., 64
Link, G., 24
Linton, L. A., 128
Löb, Walther, 8
Lochte, H. L., 104
  et al, 102
Locket, G. H., *see* Hammick, D. L.
Loeb, Morris, 87
Loewenherz, Richard, *see* Täuber, Ernst
Lonnies, Hermann, 28
Loomis, C. C., 2
Löpmann, Bernhard, *see* Ott, Erwin
Loriette, P., 60, 73
Löwenhamm, E., *see* Euler, Hans von
Lowitz, T., and Richter, D., 52

Lowry, T. M., *see* Bousfield, W. R.
Lowy, Alexander, and Dunbrook, R. F., 31
Lubs, H. A., 165
Lundén, Harald, 160

Maass, O., and Hatcher, W. H., 25
  and McIntosh, D., 36, 86
Mabery, C. F., 96, 153, 155
MacArthur, C. G., *see* Darrah, J. A.
McCallum, S. T., 44
McDaniel, A. S., 5
McElroy, K. P., *see* Krug, W. H.
McFarland, D. F., *see* Bartow, Edward
McIntosh, D., 37
  see also Archibald, E. H., *and* Maass, O.
McKee, R. H., and Berkheiser, E. J., 18, 19
  and Cable, D. E., 36
  and Holmes, A. A., 36
  and Strauss, F. A., 139
McKee, S. R., *see* Remsen, Ira
McKelvy, E. C., 51
  and Simpson, D. H., 63, 69, 70, 136
  see also Osborne, N. S.
MacKensie, K. G., 107
McKenzie, Alex, 126
Macleod, A. L., *et al*, 49
McMaster, LeRoy, 10
  and Magill, A. C., 10, 104
Magill, A. C., *see* McMaster, LeRoy
Magri, G., *see* Antony, U.
Malfatti, Hans, 44
Malmgren, S. M., 126
Mandel, J. A., *see* Friedburg, L. H.
Mandelbaum, M. R., *see* Bogert, M. T.
Mangam, A. W., and Acree, S. F., 94, 110
Mann, H., 101
Mann, M. D., 52
Mann, M. D., Jr., and Williams, R. R., 118
Mannessier, Anna, 112
Manning, R. J., 7
Marden, J. W., and Dover, M. V., 8
Mariller, C., 54, 79
Marks, E. C. R., 67
Marsh, J. E., 19
Marshall, John, 115
Martin, A. W., *see* Schlesinger, H. I.
Marvel, C. S., and Tanenbaum, A. L., 62
  see also Adams, Roger
Massini, Paul, *see* Schmidein, Julius
Matheson, H. W., 100
Mehren, 7
Mendeleeff, D., 52, 53, 57, 58, 59, 62, 73
Menschutkin, N., 10, 11
Menzies, R. C., 73
Merrell, C. G., *see* Gordin, H. M.
Merriman, R. W., 66
  see also Wade, John
Michael, Arthur, 154
  et al, 75
Michaelis, A., 100
Michaelis, Gustavus, 85
Michel, E., *see* Haller, A.
Middendorp, J. A., 150
Miner, C. S., *et al*, 101
Miyazaki, K., *see* Tomiyama, T.
Möhlau, Richard, and Fritzsche, E., 107
Moir, James, 26
Moissan, Henri, 60
Montagne, P. J., 137
Montgomerie, H. H., *see* Patterson, T. S.
Moore, F. J., 12
Moore, R. J., *et al*, 35
Moore, R. W., 13
Morgan, J. L. R., and Lammert, O. M., 105
Mortimer, F. S., 14
  and Murphy, R. V., 135
Moschatos, H., and Tollens, B., 99
Mosenthal, H. de, 7
Mott, W. R., *see* Patten, H. E.
Mueller, Max, 138
Muller, E., *see* Pinnow, Joh.
Muller, E. G., *see* Knecht, Edmund
Murdoch, D. G., and Galbraith, W. L., 110
Murphy, R. V., *see* Mortimer, F. S.
Mylius, F., 47, 78

Nádai, Géza, *see* Ullman, Fritz
Naumann, Alex., 39
Nedzati, F., *see* Schönberg, A.
Nef, J. U., 85
Nelson, J. M., *see* Griffin, E. G.
Nencki, M., 146

Nencki, M., and Sieber, N., 76
  see also Berdez, J.
Neuberg, Carl, 23, 110
Newcomb, Clive, 133
Newman, R. K., 83
Niementowski, Stefan von, 77
Noelting, Emilio, and Schwartz, Ch., 115
  and Witt, O. N., 107
Norlin, Evert, *see* Klason, Peter
Norris, J. F., 17
Nottbrack, Friedrich, 24
Noyes, A. A., and Sherrill, M. S., 4
  and Westbrook, L. R., 22
Noyes, W. A., 56, 57
  and Goebel, W. F., 50
  and Potter, R. S., 146
  and Warfel, R. R., 59
Nussbaum, Josef, *see* Bamberger, Max

Oddo, Bernardo, 108
Odèn, Sven, 131, 154
Olivier, S. J. C., 10, 137
Orndorff, W. R., and Hitch, E. F., 15
  and Kennedy, J. J., 45
Orton, K. J. P., and Bradfield, A. E., 91
  and Jones, D. C., 69, 76
  et al, 91
Osborne, N. S., and McKelvy, E. C., 51, 58, 63, 70, 72
  et al, 60, 70
Osborne, T. B., *see* Chittenden, R. H.
Ossendovsky, A. M., 78, 80
Ostromysslensky, Iwan, 4, 97, 127
  see also Zerewitinoff, Th.
Ott, Erwin, and Löpmann, Bernhard, 97
Otto, Robert, 24, 166
Oudemans, A. C., 7
Oyster, Leone, and Adkins, Homer, 27

Palkin, S., 9
Palm, R., 23
Palmer, C. S., and Adams, Roger, 135
Pardee, A. M., *et al*, 75
Partheil, A., 155
  and Rose, 87
Partington, J. R., *see* Lapworth, Arthur
Patart, Georges, 51
Patten, H. E., and Mott, W. R., 42
Patterson, A. M., 11
Patterson, T. S., and Montgomerie, H. H., 10
Paul, Joseph, 72
Pawlewski, Br., 81, 144
Peachy, S. J., 138
Peddle, C. J., and Turner, W. E. S., 131
Peligot, E., *see* Dumas, J.
Pépin-Lehalleur, 75
Perkin, A. G., 88
Perkin, F. M., and Pratt, Lionel, 60
Perkin, W. H., 53
Perkin, W. H., Jr., and Robinson, Robert, 90
  see also Haworth, Edw.
Peters, Daniel, *see* Freudenberg, Karl
Pfeiffer, P., and Würgler, J., 159
Pfitzinger, Wilhelm, *see* Wernicke, August
Phelps, E. P., *see* Rowe, A. W.
Philip, J. C., 159
  and Garner, F. B., 159
Philips, A., *see* Graebe, C.
Phillips, B., 100
Piettre, Maurice, 109
Pinner, A., 100
Pinnow, Joh., and Muller, E., 134
  and Pistor, G., 166
Pique, René, 51, 56, 66
Pistor, G., *see* Pinnow, Joh.
Plauson, H., 35
Plücker, W., 51, 73
Poleck, Th., and Thümmel, K., 85
Pope, W. J., and Turner, E. E., 100
  see also Harris, J. E. G.
Posternak, S., 18
Potter, R. S., *see* Noyes, W. A.
Powell, W. J., *see* Ingold, C. K.
Pozzi-Escot, Emm., 63
Pratt, Lionel, *see* Perkin, F. M.
Prentiss, S. W., 10
Prescott, A. B., *see* Knox, J. W. T.
Prisley, Frederic, *see* Read, R. R.
Pritchett, R. H., *see* Bailey, J. R.
Pucher, Geo. W., and Dehn, W. M., 44
  and Johnson, T. B., 104

Quam, G. N., 37
Quick, A. J., 31

Raffo, M., and Rossi, G., 112
Rappenstrauch, G. A., 24
Rathjen, A., *see* Jannasch, P.
Read, John, and Hurst, Eric, 141
Read, R. R., and Prisley, Frederic, 117
Reade, T. H., and Sim, S. A., 45
Reichert, E. T., 166
Reid, E. W., *see* Curme, G. O., Jr.
Reimer, K., and Tiemann, Ferd., 1
Remler, R. F., 104
Remsen, Ira, and McKee, S. R., 115
Remy and Erhart, 96
Renshaw, R. R., and Holm, G. E., 9
Rheinheimer, Wilhelm, *see* Wieland, Heinrich
Richardson, Clifford, and Forrest, O. N., 133, 134
Richter, D., *see* Lowitz, T.
Riddle, R. N., 101
Riedel, J. D., 27
Riederer, H. S., *see* Baskerville, Charles
Riiber, C. N., 64, 72
Ritschke, A., *see* Gattermann, Ludwig
Ritsert, Eduard, 24
Rivett, A. C. D., and Rosenblum, E. I., 160
Roberts, H. M., and Bury, C. R., 139
Robertson, H. C., and Acree, S. F., 61, 70
Robinson, Robert, *see* Perkin, W. H., Jr.
Robinson, W. S., *see* Jackson, C. L.
Robison, Robert, *see* Hantzsch, A.
Rodebush, W. H., 67
Roemer, H., *see* Schunck, E.
Römer, G., *see* Schenck, Rudolf
Rose, *see* Partheil, A.
Rosenblum, E. I., *see* Rivett, A. C. D.
Rossi, G., *see* Raffo, M.
Roulleux, M., and Dort, R. G., 99
Rowe, A. W., 83
  and Phelps, E. P., 71, 83
Rudberg, Karin, *see* Euler, Hans von
Ruhemann, S., 45
Rule, H. G., 6
Rümpler, A., 157
van Ruymbeke, Joseph, 54
Ruzicka, L., and Trebler, H., 126

Sachs, Franz, 39, 102
Sagrebin, W., 11
St. Gilles, L. Péan de, 39, 102
  see also Berthelot, M.
Salkowski, E. and H., 87
Sawyer, H. L., *see* Hudson, C. S.
Schär, Ed., 12, 89
Schenck, Rudolf, and Römer, G., 8
Schiebler, Helmuth, *see* Fischer, Emil
Schierz, E. R., 95
Schiff, Hugo, 43, 87
Schlesinger, H. I., and Calvert, R. P., 95
  and Martin, A. W., 95
Schlieper, F. W., 30
Schmidlin, Julius, and Massini, Paul, 18
Schmidmer, Eduard, *see* Fischer, Emil
Schmidt, Ernst, 132
Schmidt, J. H., 92, 120
Schmitt, Gerhard, 35
Schneible, Joseph, 55
Schoepfle, C. S., *see* Gomberg, M.
Scholl, Roland, and Berblinger, Hans, 112
Scholtz, M., 45, 105
Scholvein, L., 150
Schönberg, A., and Nedzati, F., 139
Schöpff, M., 17
Schraube, Conrad, 107
Schultess, O., *see* Graebe, C.
Schultz, G., 26
Schunck, E., and Roemer, H., 23
Schwalbe, C., 122
Schwartz, Ch., *see* Noelting, Emilio
Scott, W. B., *see* Jennings, W. L.
Seidel, Paul, 139
Seidell, Atherton, 41
Seidenberg, Armin, 38, 157
Semper, Leopold, and Lichtenstadt, Leo, 46
Seyer, W. F., *see* Krieble, V. K.
Seyewitz, A., *see* Liebermann, C.
Sherk, D. C. L., *see* Kremers, Edward
Sherman, H. C., and Tanberg, A. P., 163
Sherrard, E. C., and Froehlke, A. W., 30
Sherrill, M. S., *see* Noyes, A. A.
Shipsey, Kathleen, and Werner, E. A., 102, 105
Sidgwick, N. V., and Spurrell, W. J., 48
Sidot, Th., 136
Siebenrock, E. von, 84
Sieber, N., *see* Nencki, M.

Siebert, Sigurd, *see* Speyer, Edmund
Sim, S. A., *see* Reade, T. H.
Simon, S. E., 43
Simpson, D. H., *see* McKelvy, E. C.
Sisley, P., 132
Skellon, H., 121
Sloan, A. W., *see* Conant, J. B.
Smith, G. F., 75
Smith, J. L., 55, 56
Smith, L. B., *see* Taylor, R. S.
Smith, L. I., *see* Kohler, E. P.
Smithey, I. W., *see* Wheeler, A. S.
Snyder, J. P., 134
Somerville, J. L., 48
Soubeiran, E., 52, 57, 58
Soutar, C. W., *see* Atack, F. W.
Spenzer, J. G., 140, 150
Speyer, Edmund, and Sibert, Sigurd, 152
Spurrell, W. J., *see* Sidgwick, N. V.
Squibb, E. R., 57, 62, 92
Staedel, Wilhelm, 125
Stafford, O. F., *see* Franklin, E. C.
Stäger, Hans, 45
Stanbridge, Fred'k, 47
Steele, B. D., *et al*, 36
Steffens, J. A., 67
Stenhouse, John, and Groves, C. E., 29
Stock, Alfred, 32
Strauss, F. A., 140
  see also McKee, R. H.
Stuckgold, M., 39
Sullivan, F. W., Jr., *see* Gomberg, M.
Sunde, Einar, *see* Goldschmidt, H.
Svanberg, Olaf, *see* Euler, Hans von
Swensson, Torsten, 47

Tabern, L., *see* Gomberg, M.
Tanberg, A. P., 108, 109
  see also Sherman, H. C.
Tanenbaum, A. L., *see* Marvel, C. S.
Täuber, Ernst, and Loewenherz, Richard, 119
Tausz, Jenö, 97
Taylor, R. S., and Smith, L. B., 83
Tharaldsen, C. E., 101
Thiele, Johannes, and Dimroth, Otto, 81
Thompson, T. G., *et al*, 50
Thoms, H., 150
Thomson, Andrew, *see* Carnelly, Thomas
Thorin, E. G., 160
Thorne, P. C. L., 162
Thorpe, J. F., *see* Cain, J. C.
Thuesen, Arthur, *see* Goldschmidt, Heinrich
Thümmell, K., *see* Poleck, Th.
Tiemann, Ferd., and Krüger, Paul, 116
  see also Reimer, K.
Tingle, J. B., and Bates, S. J., 152
Tollens, B., *see* Moschatos, H.
Tomiyama, T., and Miyazaki, K., 135
Torrey, H. A., and Brewster, C. M., 154
Traub, M. C., 2
Trebler, H., *see* Ruzicka, L.
Truhlar, Joseph, 124
Tschelinzeff, W., 126
Tsujimoto, Mitsumaru, 103
Tubandt, C., 11
Turner, E. E., *see* Pope, W. J.
Turner, W. E. S., and Bissett, C. C., 41, 42
  see also Peddle, C. J.
Tyrer, Dan, 151

Ullman, Fritz, and Nádai, Géza, 16
Ulpiani, C., 152
Ulsar, L. von, and Erdmann, J., 77
Underwood, H. W., Jr., and Kochmann, E. L., 93
Urbain, E. and R., 67

Valenta, E., 138
Valli-Douau, L., 74
Van den Berg, L. M., 131
Vandevelde, A. J. J., 78
Van Sicklen, W. J., *see* Young, S. W.
Varma, P. S., and Kulkarni, D. A., 104
von Veimarn, P. P., 42, 158
Venable, C. S., and Fuwa, Tyler, 121
  and Greene, C. D., 121
Vender, Vezio, 28
Verley, A., and Bölsing, Fr., 111
Verola, P., *et al*, 53
Vesely, Viktor, and Votocek, Emil, 27
Vignon, L., 139

Vignon, L., and Evieux, E., 125
Vincent, C., and Delachenal, 59
Vis, G. N., 104
Voit, Erwin, 87
Voss, H., 137
Votocek, Emil, *see* Vesely, Viktor

Wacker, Alexander, 135
Wade, John, and Finnemore, Horace, 22, 84
  and Merriman, R. W., 66
Walden, P., 4, 34, 97
  and Centnerszwer, M., 4
Wales, H., 30
Walker, J. W., *et al*, 37
Wallach, O., 12
  and Brass, W., 81
Waller, E., 70
Walther, R. von, and Hübner, R., 3, 93
Walton, J. H., and Lewis, H. A., 25, 112
  and Wise, C. R., 6
  and Withrow, L. L., 97
Warfel, R. R., *see* Noyes, W. A.
Warren, W. H., 56
Wartha, V., 101
Wedekind, E., 88
  and Haussermann, J., 88
Weehuisen, F., 118
Weil, Hugo, *see* Landauer, Paul
Weill, S., *see* Holde, D.
von Weimarn, P. P., *see* von Veimarn, P. P.
Weinberg, Arthur, 165
Weinhaus, Heinrich, 166
Weiss, M. L., 125
Weissgerber, R., 26
  see also Knoevenagel, E.
Weitenkampf, Carl, 167
Wenzel, G., 137
Werner, E. A., *see* Shipsey, Kathleen
Wernicke, August, and Pfitzinger, Wilhelm, 93
West, B. L., 10
Westbrook, L. R., *see* Noyes, A. A.
Wheeler, A. S., 126
  and Bost, R. W., 153
  and Smithey, I. W., 93, 127
Wherry, E. T., *see* Jamieson, G. S.
White, G. F., 33
  see also Kraus, C. A.
Wieland, Heinrich, 116
  and Rheinheimer, Wilhelm, 16, 107
Wightman, E. P., *et al*, 57
Wilcox, W. G., 108
Wildermann, Mejer, 71
Will, H. R., *see* Knox, Jos.
Will, W., 30, 101
Williams, P. N., *see* Brady, O. L.
Williams, R. R., *see* Mann, M. D., Jr.
Williamson, A., 148
Wilson, D. C., 148
Wilson, R. E., 22
  and Fuller, E. W., 137
Willstätter, Richard, 47
  and Bolton, E. K., 92
  and Jaquet, Daniel, 93
Wilton, Thomas, 33
Windaus, A., and Klänhardt, F., 140
Windisch, W., 72
Winkler, L. W., 60, 62, 71, 73, 74
Winninghoff, W. J., *see* Keyes, F. G.
Wirth, Ernst, 124
Wise, C. R., *see* Walton, J. H.
Wislicenus, Hans, and Kaufmann, Ludwig, 63
Wislicenus, Johannes, 116
Wislicenus, Wilhelm, and Erbe, Rudolf, 17
Withrow, L. L., *see* Walton, J. H.
Witt, O. N., 23, 98
  see also Noelting, Emilio
Witter, H., *see* Büchner, Eduard
Wolff, Carl, 141
Wollenberg, H. L., and Bigelow, C. A., 23
Wood, H. C., Jr., 48
Würgler, J., *see* Pfeiffer, P.
Wyrouboff, G., 19

Yoder, Lester, *see* Dox, A. W.
Young, C. O., *see* Curme, G. O., Jr.
Young, J. G., *see* Ewan, Thos.
Young, S. W., 145
  and Burke, W. E., 147
  and Cross, R. J., 145
  and Van Sicklen, W. J., 145
Young, Sidney, 53, 66, 119

Young, Sidney, and Fortey, E. C., 51
Yvon, P., 65

van der Zande, J. E., *see* von Itallie, L.
Zechmeister, László, *see* Bjerrum, Niels
Zerewitinoff, Th., 90, 108, 109, 127
  and Ostromysslensky, Iwan, 109
Zetter, Georg, 9
Zierold, Georg, 99
Zwenger, Constantin, 128

INDEX OF SOLVENTS

Acetamide, 97
Acetic acid, 91, 124
Acetic anhydride, 97
Acetone, 39, 97, 101
Acetone-sulfur dioxide, 35
Acetophenone, 105
Acetylene, chlorination products of, 135
Alcohol, 2, 40, 50
  see also names of individual alcohols
Alcoholic acid or ammonia, 49
Aldehydes, 101
Aliphatic hydrocarbons, 114
Allyl alcohol, 78
Amines, 106
  see also names of individual amines
Ammonia (liquid), 32
Amylal, 101
Amyl alcohol, 76, 153
Aniline, 106
Anisol, 90
Aromatic hydrocarbons, 122
  see also names of individual hydrocarbons
Azobenzene, 139

Benzene, 16, 122
Benzine, 117, 134
Benzyl benzoate, 101
Benzyl cinnamate, 101
Bromobenzene, 136
Bromotoluene, 136
Butyl alcohol, 74

Carbon dioxide (liquid), 37
Carbon disulfide, 10, 129, 136
Carbon tetrachloride, 133, 140
Chlorinated hydrocarbons, 129
Chlorination products of acetylene, 135
Chlorobenzene, 135
Chloroform, 130
Colophony, 97
Cumene, 127
Cymene, 126
Cyneol, 81

Decacyclene, 127
Dichlorobenzene, 135
Dichloroethylene, 135
Dichlorhydrin, 81
Dimethyl aniline, 107
Dimethyl ether, 89
Dimethyl sulfate, 138

Epichlorhydrin, 81
Esters, 100
  see also names of individual esters
Ethers, 82
  see also names of individual ethers
Ethyl acetate, 7, 104
Ethyl alcohol, 45
Ethyl benzoate, 101
Ethyl chloride, 130
Ethylene bromide, 130
Ethylene glycol, 78
Ethyl ether, 82
Ethyl formate, 117

Formamide, 97
Formic acid, 95
Furfural, 101

Gasoline, 119
Glycerol, 78

Halogen acids, 30
Heptane, 120
Hexane, 116
Higher alcohols, 74
  see also names of individual alcohols.
Higher ketones, 104
Hydrocarbons, 114
  see also names of individual hydrocarbons
Hydrobromic acid, 31

Hydrochloric acid, 30, 31
Hydrofluoric acid, 31
Hydrogen bromide (liquid), 36
Hydrogen chloride (liquid), 36
Hydrogen peroxide, 24
Hydrogen sulfide (liquid), 37

Inorganic acids, 25
Inorganic salts, solutions of, 23
Isoamyl chloride, 130
Isoamyl ether, 90
Isobutyl alcohol, 75
Isobutyl chloride, 130
Isopropyl alcohol, 74
Isopropyl chloride, 130

Kerosene, 117
Ketones, 101

Ligroin, 115
Liquefied gases, 32
Liquid paraffin, 118

Mesitylene, 127
Methylal, 90
Methyl alcohol, 45
Methylamine, 106
Methyl bromide, 130
Methyl chloride, 130
Methyl diphenylamine, 107
Methyl formate, 117
Monobromonaphthalene, 136

Naphthalene, 127
Naphthol ethyl ether, 98
Nitric acid, 29
Nitrobenzene, 90, 138

Oleic acid, 96
Organic acids, 91
  see also names of individual acids
Organic bases, 105
  see also names of individual bases

Paraffins, 114
  see also names of paraffin fractions
Petroleum ether, 115
Phenol, 8, 98
Phosgene, 98
Picolines, 108
Propyl alcohol, 74
Pyridine, 7, 39, 107
Pyridine bases, 112

Quinaldine, 113
Quinoline, 44, 112

Rubber hydrocarbon, 121

Selenium oxychloride, 37
Spermaceti, 101
Stearic acid, 96
Sulforicinic acid, 96
Sulfur dioxide, 34
Sulfuric acid, 25

Tetrachloroethane, 8
Tetrachloroethylene, 135
Thiophene, 125
Toluene, 9, 125
Trichloroethylene, 135
Turpentine, 128

Water, 21

Xylene, 9, 126

INDEX OF SUBJECTS

Abietic acid, 154
Absolute alcohol, affinity for moisture of, 73
  preparation of, 51
Acenaphthene, 127
Acetaldehyde, 100, 135
Acetamide as solvent, 97
Acetanthranilic acid, 92
Acetic acid, 118
  as solvent, 91, 124
  drying of, 91
Acetic anhydride as solvent, 97
Acetoacetic ester, 89
Acetone as solvent, 101
  for petroleum extraction, 97
  for reactions with permanganate, 39
  sulphur dioxide mixture as solvent, 35
Acetophenone as solvent, 105
Acetylamino benzoic acid, 20
Acetylene, chlorination products of, as solvents, 135
Acid chlorides, 32, 88, 131, 141
Acylglucoside, 154
Adjuvance, 10
Albumen, 157, 166
Albumoses, 97
Alcohol, analytic determination of, 163
  as solvent, 2
  as solvent, esterification with, 10
  as solvent for extractions, 50
  negative catalysis by, 47
  preparation of neutral, 73
Alcohols as solvents for inorganic compounds, 40
  estimation of water in, 67
  removal of aldehyde from, 70
  salting out of, 162
  solubility in aqueous potassium carbonate, 50
Alcoholic acid or ammonia as solvent, 49
Aldehyde ammonia, 100
Aldehyde, removal from alcohol, 70
Aldehydes, as solvents, 101
  synthesis of aromatic, 2
Aliphatic hydrocarbons as solvents, 114
Alizarin, 96
  green, 139
Alkaloids, 77, 89, 92, 105, 109, 116, 132, 163
  see also names of individual alkaloids
Alkyl iodides, 103
Allyl alcohol, addition product with barium oxide, 60
  as solvent, 78
  iodide, 140
  tetramethoxy benzene, 150
Aluminum amalgam as drying agent for alcohols, 63
Amidoindigo, 165
Amidophthalic ester, 165
Amines as solvents, 106
Aminoacetochloroanilide, 150
Amino acids, 159
Aminoanthraquinone, 106
Aminoazo toluene, 107
Aminodehydrocampholytic acid, 146
Aminophenol, 139
Amidophenyloxytrichloroethane, 99
Ammonia as solvent, 32
Ammonium acetate, 50
  chloride as precipitant, 165
  oxalate as precipitant, 166
  quaternary perhalide, 45
  salts of weak acids, 9
  sulfate as precipitant, 166
Ammono-carbonic acids, 32
Amorphous substances, purification of, 143
Amylal as solvent, 101
Amyl alcohol as solvent, 76, 153
Amylase, 163
Angelic acid, 116
Aniline, 125
  as solvent, 106

Aniline tellurium tetrabromide, 31
Anisaldoxime, 11
Anisol as solvent, 90
Anisolazoxyphenetol, 96
Anthocyanines, 92
Anthracene, 16, 27, 33, 36, 96, 98, 105, 112, 124, 135, 150
Anthraquinone, 98, 118, 135, 139
Arabic acid, 157
Aromatic hydrocarbons as solvents, 122
  purification of, 122
Aromatic sulfonic acids, 27
Arsenic compounds, 93
Arsphenamine, 166
Asphalt, 128, 134
Asphaltenes, 128
Atmolysis, 67
Azobenzene, 29, 121
  as solvent, 139
Azo derivatives, reduction of, 110
  dyestuffs, 26
Azoxyanisol, 96
Azoxyphenetol, 96

Barium acridone sulfonate, 17
  choleate, 47
  oleate, 123
  oxide as drying agent for alcohols, 59
  oxide as drying agent for pyridine, 108
Bebeerin, 45
Benzaldoxime, 151
Benzamarone, 101
Benzanthrone, 118, 135
Benzene as solvent, 16, 117, 122, 134
  distillation method for drying pyridine, 109
  distillation method for preparing absolute alcohol, 66, 76
  effect of moisture in, 123
  monosulfonic acid, 163
  of crystallization, 124
  purification of, 81
  solubility of, in alcohol, 48
Benzoic acid, 2, 15, 16, 125, 138, 159
  mixed crystals with cinnamic acid, 20
Benzonitrile, 28, 29, 139
Benzophenone, 137
Benzyl alcohol, preparation of, 10
Benzylazide, 107, 127
Benzyl benzoate as solvent, 101
  chloride, 2
  cinnamate as solvent, 101
Berberin, 132
Bismuth benzoate, 79
Bitumen, 107, 128, 134
Borax solution as solvent, 23
Boric acid, 87
  anhydride, 95
Brègeat process, 99
Brine for salting out, 162
Bromacettoluide, 6
Bromobenzene as solvent, 136
  sulfone chloride, 137
Bromocarboxylic acids, 95
Bromodinitrophenylacetic acid, 17, 28
Bromohexahydrobenzoic acid, 95
Bromomethylene violet, 90
Bromomethylphthalimid, 104
Bromonitrophenol, 30
Bromophenyl cyclohexane, 141
Bromotoluene, 31
  as solvent, 136
Bucco-camphor, 87
Butter, analysis of, 78
Butyl alcohol, 118
  as solvent, 74
Butyl salicylate, 76

Caffeine kolatannate, 163
Caffeine sulfate, 49
Calcium, 60
  carbide, 65
  hydride, 64
  hydroxide, 58
Camphene, 96
Camphor derivatives, 96
Carbamide derivatives, 93
Carbazole, 16, 28, 98, 112, 135
Carbon dioxide as precipitant, 167
  liquid, as solvent, 37
Carbon disulfide, 122
  as solvent, 129, 136
  as solvent for nitrogen trioxide, 10
Carbon tetrachloride as solvent, 133, 140
Carbopyrrolic acid, 128
Carboxylic acid chlorides, 141
Carnallite, 85
Carvacrol, 119

Casein, 104
Caustic fusion, 106
Celluloid, 81
Cellulose nitrates, *see* Nitro cellulose
Cellulose, solvents for, 23, 30
Ceresin, 136
Chloral hydrate, 99
Chloramine orange, 79
Chlorhydrin, 164
Chlorinated hydrocarbons as solvents, 129
Chlorination of methane and ethane, 1
  products of acetylene as solvents, 135
Chlorobenzene as solvent, 135
Chlorobutyric ester, 130
Chloroform as solvent, 130
  for removing impurities from alcohol, 72
  reaction with, 132
Chlorohydurilic acid, 28
Chloronitrotolunitrile, 141
Chlorophenyl sulfone, 10
Chlorophyll, 47
Chlorosulfonic acid, 135
Choleic acid, 17
Cholesterilin, 128
Cholesterol, 105
Cholic acid, 50, 75, 78, 155
Chromic acid, oxidations with, 93
Cinchonidine hydrobromide, 19
Cinchonine metaphosphate, 98
  solubility of, 7
Cinnamic acid, 20
Citric acid, 18
Cocaine, 116
Codeine, 148
Cold fractionation of petroleum, 153
Colophony, 154
  as solvent, 97
  see also Rosin
Common-ion effect, 158
Conchairamine, 19
Copal, 81
Copper sulfate, 43
Cork stoppers, contamination by, 85
Cresotinic acid, 104
Critical solution temperature, 69, 76, 78
Crystallization, 12
  means of inducing, 143
Crystallization, theory of, 144
Cumene as solvent, 127
Cyanic acid, 93
Cyanogen chloride, 140
Cymene, 93
  as solvent, 126
Cyneol as solvent, 81
Cytistin, 155

Decacyclene as solvent, 127
Dehydration of alcohols, theory of, 55
Dehydrocholic acid, 46
Deoxyalizarin, 88
Diacenaphthalene azotide, 139
Diacetoamine, 104
Diacetyl ethylene diamine, 107
Dialysis, 110
Diaminoanthraquinone, 106
Diaminodiphenylamine, 29
Diamino oxyphenyltolyl sulfonic acid, 165
Diazo compounds, 45, 99
Diazoamino benzene, 118
  toluene, 107
Dibromodinaphthyl oxide, 125
Dibromopentane, 28
Dichlorobenzene as solvent, 135
Dichlorodinitrophenylacetic acid, 28
Dichloroethylene as solvent, 135
Dichloroethyl sulfide, 50
Dichlorohydrin as solvent, 81
Dichlorophthalic anhydride, 152
Dicyanine, 9
Diethylamine, 157
Diethylammonium mercuric iodide, 156
Diethyl phenol, 88
Differential evaporation, 156
Diggers pine, 120
Digitalin, 48
Digitonin, 48
Dihydropyridine, 109
Dihydroxybenzanthrone, 88
Dihydroxy naphtholic acid, 119
Dilution with non-solvent, 151
Dimethyl aniline as solvent, 107
  ether as solvent, 89
  homophthalimide, 116
  sulfate as solvent, 138

Dinaphthyl oxalic ester, 124
Dinitrobenzophenone, 125
Dinitro dichlorobenzene, 49
  ditolyl, 119
  stilbene, 81
  tetrachlorofluoran, 45
  toluene, 30
Diphenic acid, 93
Diphenyl ether, 99
Diphenylguanidine, 125
Diphenylnaphthol pyrazoline, 154
Dithiosulfindene, 112
Drugs, 89, 92
  see also Alkaloids
Dyestuffs, 24, 109, 118, 139, 158, 162, 165

Eleagic acid, 110
Emulsions, 87, 132
Epichlorhydrin as solvent, 81
Essential oil, 119
Esterification, 111
  constant, 68
Esters, 32
  as solvents, 100
Estimation of water in alcohols, 67
Ethane, 1
Ether, drying with sodium hydroxide, 52
  effect of water on solvent powers of, 87
  evaporation and distillation of, 89
  inhibiting crystallization by, 154
  purification of, 83
  reactivity of, 88
  removal of peroxide from, 89
  salting out of, 162
Ethereal solutions, drying of, 84
  oils, 115
Ethers as solvents, 82
Ethyl acetate as solvent, 7, 104
  acetate, detection of water in, 86
  alcohol as solvent, 45
  alcohol, reaction with solvent, 45
  benzoate as solvent, 101
  bromide, 27
  chloride, 152
  chloride as solvent, 130
  butyl ether, 88
  ether as solvent, 82
  formate as solvent, 117
  iodide, 48
Ethylene bromide as solvent, 130
  glycol, 15
  glycol as solvent, 78
Eurhodol, 98
Extraction media, 133

Fats, 137, 157
  extraction of, 87, 130, 134
  saponification of, 74, 117
Fatty acids, 38, 46
Fish oils, 103
Fluorobenzene sulfonic acid, 30
Formamide as solvent, 97
Formic acid as solvent, 95
Formylamino dimethyl aniline, 166
Formylphenylacetanilide, 17
Formylphenylacetic ester, 154
Fractional freezing, 149
Friedel-Crafts reaction, 117, 137
Fructose, 95
Furfural as solvent, 101
Furfuralcohol, 166
Fusel oil, 167

Gall, 156
Gallotannic acid, solubility of, 7
Gases, solubility of, 5, 121
Gasoline as solvent, 119
  precipitation by, 152
Gelatin, 157
Ginger, essential oil of, 119
Glass rod, rubbing with, to induce crystallization, 144
Glucose, 94, 110
Glucoside, 131
Glutaric acid, 140
Glycerides, 157
Glycerol as drying agent for alcohols, 54
  as solvent, 78
Glycocholic acid, 156
Glycocoll, 79
Glycollic acid, 104
Glyoxalone, 47
Grape sugar, 19, 20
Graphite, 127
Grignard reaction, 87, 108
  reagent, 87, 90, 108, 126, 127
Gum arabic, 157

Halochromy, 26
Halogen acids as solvents, 30
Helianthine, solubility of, 7
Hemin, 76
Heptane as solvent, 120
Hexachloroethane, 133
Hexaethylbenzene, 13, 88
Hexahydrobenzene, 124
Hexamethylene amine, 99, 119
Hexane as solvent, 116
  isolation of, 119
  solubility in alcohol, 48
Higher alcohols as solvents, 74
  ketones as solvents, 104
Homopinocamphoric acid ester, 126
Humus, 109
Hydrastin, 132
Hydrobromic acid as solvent, 31
Hydrocarbons as solvents, 114
  stearic acid as solvent for, 96
Hydrochloric acid as solvent, 30, 31
Hydrocupreine, 152
Hydrocyanic acid, 93
Hydrofluoric acid as solvent, 31
Hydrogenation, 93
Hydrogen bromide and chloride (liquid) as solvents, 36
  peroxide, 112
  peroxide as solvent, 24
  peroxide in ether, explosive effect of, 89
  sulphide, liquid, as solvent, 37
Hydroquinine, 105
Hydrosulphite, extraction with, 118
Hydrotropy, 23, 160
Hydroxy anthraquinoline, 139
Hydroxybenzalphenyl ethylamine, 51
Hydroxybenzoic acid, 20
Hydroxylamine, 75, 153
Hydroxyphenyl-azo-hydrocupreine, 74, 165
Hyoscine hydrobromide, 47
Hypochlorite for removing acetone from methyl alcohol, 73

Indanthrene, 112
Indene, 141
Indigo, 96, 97, 98, 101, 112, 119, 128, 138
Inert liquids as solvents, 129
Inisitohexaphosphoric acid, 18
Inoculation 147
Inorganic acids as solvents, 25
  salts, solutions of, as solvents, 23
  salts, organic solvents for, 38
Inosite, 94
Interliquefaction, 11
Iodides, alkyl, 103
Isoamyl chloride as solvent, 130
  ether as solvent, 90
  quinazolone methyl ether, 148
Isobutyl alcohol as solvent, 75
  chloride as solvent, 130
Isobutylene, 117
Isoharman, 90
Isophthalic acid chloride, 146
Isopropyl alcohol as solvent, 74
  chloride as solvent, 130

Jamaica ginger, 163

Kerosene as solvent, 117
Ketones as solvent, 101
Kieselguhr as diluent, 141
Kola nuts, 163
  tannin, 101, 163

Lecethin, 88
Leucine, 49
Leuco methylene blue, 119
Leukacene, 127
Light oil, 122
Ligroin as solvent, 115
Lime as drying agent for alcohols, 55
Liquefied gases as solvents, 32
Liquid crystals, 96, 136
  paraffin as solvent, 118
Lithium chloride, 6, 8
Logwood, 105

Magnesium, 62
  amalgam, 64
  hydroxide, 58
  sulfate, 19
Malonic ester, 137
Malonitrile as solvent, 97
Maltose, 146
Mandeliminohydrin, 6

Mannose, 94
Mass action, 159
Mayer's reagent, 157
Mechanical means for inducing crystallization, 144
Mercuric fulminate, 152
Mercury, alkali double iodide, 19
  halides, 38
Mesitylene as solvent, 127
Methane, 1
Methoxybenzophenone, 137
Methylal, 103
  as solvent, 90
Methyl alcohol as solvent, 45
Methylamidocrotonic anilide, 101
Methylamine as solvent, 106
Methyl bromide as solvent, 130
  chloride as solvent, 130
  diphenylamine as solvent, 107
Methylene blue, 98
  leuco, 119
  ditolyl triamido toluene, 148
  red, 98
Methylethyl ketone, 104
Methyl formate as solvent, 117
  magnesium iodide, *see* Grignard reagent
  malonic ester, 126
  uramidobenzoyl, 77
  violet, 141
Milk analysis, 130
Mineral oils, 45
Mixed crystals, 19
Molybdenum xanthate, 131
Monoamino acids, 75
Monobromocamphor, 126
Monobromonaphthalene as solvent, 136
Morphine, 77, 132
Murexide, 165
Musk, 101
Mustard gas, 50

Naphthalene, 24, 121, 126, 151
  as solvent, 127
  diamine, 8
  monosulfonic acid, 126
  sulfonic acids, 23, 30
Naphthionic acid, 127
Naphthol, 135
  ethyl ether as solvent, 98
Naphthoquinone sulfonic acid, 113
Naphthylamine sulfonic acid, 127
Neutral alcohol, preparation of, 73
Nickel sulfate, 19
Nicotine, 135
Nitraniline, 89, 134
Nitric acid as solvent, 29
Nitrobenzazoxazin carboxylic acid, 46
Nitrobenzene, 110
  as solvent, 90, 138
Nitrobenzoic acid, 20
Nitrobenzonitrile, 134
Nitrobenzyl phthalimid, 141
Nitrosocarbazol, 124
Nitrocellulose, 81, 101
  solvents for, 7, 33
Nitrochloroaniline, 6
Nitrochlorophenol, 153
Nitro cyclopropane, 148
  cymene, 93
  diazoaminobenzene, 81
  dichloronaphthalene, 79
Nitrogen trioxide, 29, 136
Nitroguanidine, 27
Nitronaphthacene quinone, 101
Nitrophenetol, 27
Nitrophenol, 30
Nitroso dimethylaniline, 107, 113
Nitrosoörcin, 29
Nitrotoluene, 147, 149
Nitrotoluidine, 88
Nitrotyrosine hydrochloride, 30

Oak tannin, 110
Oils, 103, 106, 157
Oleic acid as solvent, 96
Organic acids as solvents, 91
  bases as solvents, 105
Organomagnesium compounds, *see* Grignard reagent
Osazones, 110
Overlaying with non-solvent, 155
Oxalic acid, 95
Oxalyl chloride, 111
Oxidation with chromic acid, 93
Oxyhemoglobin, 113, 125, 166
Oxymethylfurfurol, 150

Paraffin, 153
  crystallization of, 14, 144
  precipitation of, from tar, 104
Paraffins as solvents, 114
Parahemoglobin, 146
Pararosaniline, 115
Parsley oil, 150
Partial evaporation, 146
Partition coefficient, 112
Pentabromoacetone, 46
Pentanes, isolation of, 119
Peptide anhydrides, 75
Peptones, 97, 157, 166
Per-acids, 150
Petroleum ether as solvent, 115
  purification of, 35, 81
  residue, 153
Phenanthrene, 9, 16
Phenanthraquinone, 27
Phenarsazine, 16, 107
  oxide, 92
Phenol, 104
  addition products with, 99
  as solvent, 8, 98
  hydrate, 148
  acetate as solvent, 101
Phenoxybutyl alcohol, 62
Phenylamino acetonitrile, 3
Phenylammonium salt, 103, 155
Phenylarsine, 135
Phenyl butene ester, 148
  glucosazone, 90
  hydrazine, 24, 132
  indazole, 116
Phenylene diamine, 31, 71
Phloretin, 87
Phlorizine, 109
Phosgene, 100, 137
  as solvent, 98
Phosphorus oxychloride, 125
  pentoxide, 63
  trichloride, 63
  trioxide, 95
Phthalic acid, 160
  anhydride, 134
Phthalimide, 77, 93
Phthalimidobenzylsulfonethylenediamine, 92
Phytosterol, 97
Picolines as solvents, 108
Picric acid, 16, 61
Pinacone, 22
Pinene, *see* Turpentine
  nitrosochloride, 96
Piperazine, 107
Piperidine, 120, 132
Piperonal, 12
Platinum black, 87
Potassium amide, 33
  carbonate as precipitant, 166
  hydroxide, alcoholic solutions of, 44
  hydroxide as precipitant, 166
  perchlorate, 75
  permanganate, 71
  phthalimide, 141
  polyiodides, 139
Proline, 75
Propyl alcohol, 118
  alcohol, addition product, 52
  alcohol as solvent, 74
Propylidene-acetic acid, 150
Proteins, 104
Protocatechuic acid, 20
Purpurin, 23
Pyridine, 131
  as solvent, 7, 39, 107
  bases as solvents, 112
  reactivity of ether with, 88
Pyrrol, 128

Quinaldine as solvent, 113
Quinine, 132
Quinoline, 26, 27
  as solvent, 112

Resins, 36, 81
Rochelle salts, 13
Rubber analysis, 101
  hydrocarbon as solvent, 121

Safranine, 133
Salicylid, 131
Salting out, 158
  effect of various salts, 160
  with brine, 162
Salts as drying agents for alcohols, 52
Sand as diluent, 139
Sandalwood oil, 48

Sandmeyer reaction, 134
Saponification, 75
Scammony resin, solubility in ether, 6
Schiff's bases, 12, 52
Selenium oxychloride as solvent, 37
Silicon tetramethylate, 63
Silver nitrate, 71
  oxide, 71
  perchlorate, 39, 123
Skraup's reaction, 115
Soap solutions, solvent action of, 24
Sodium, 33, 62, 126
  acetate, 159, 165
  benzene sulfonate, 139
  bromide, 123
  chloride, 141
  cyanide, 139
  formate, 159
  hydroxide as precipitant, 166
  iodide, 87, 102, 103
  naphthalene sulfonate, 162
  naphthionate, 127
  naphtholate, 118
  perchlorate, 75
  picrate, 52
  salicylate, 159
  sulfate as precipitant, 164
Solid diluents, 139
Solubility, rules for, 4
Solvents, chemical action with solute, 10, 16, 137
  choice of, 13
  desirable characteristics of, 100
  effect of purity of, 7
  effect of boiling-point of, 8
  effect of, on yield, 9
  effect of, on reaction velocity, 10
  for extraction, 133
  of crystallization, 17, 47
  purposes of, 3
  see also Index of Solvents, pp. 207–8
Solvent recovery, 99
Spermaceti as solvent, 101
Stearic acid as solvent, 96
Stereoisomers, 81
Stilbene dyestuffs, 81
Strychnine, 77
Sugars, 93, 109
Sulfanilic acid, 6, 18, 30
Sulfinic acids, 166
Sulfite turpentine, 126
Sulfobenzoic acid, 115
Sulfoisophthalic acid, 28
Sulforicinic acid as solvent, 96
Sulfur compounds, 112
  dioxide as solvent, 34
  dyestuffs, 158
Sulfuric acid as solvent, 25, 29
Sulfur, solubility of, in rubber, 121
  trioxide, 34
Supercooling, 18, 145, 147

Tannic acid, 100, 110, 163
Tartaric acid, 161
Tauric acid, 50
Taurocholic acid, 156
Terephthalic acid, 96
Tetrachlorodihydroxy ketoheptane, 21
Tetrachloroethane as solvent, 8
Tetrachloroethylene as solvent, 135
Tetrachlorofluorescein carbinolcarboxylic acid, 15
Tetraethyl phenol, 88
Tetrahydrofurfuralcohol, 166
Tetrahydronaphthalene, 126
Tetraiodofluorescein diacetate, 136
Tetranitronaphthalene, 30, 101
Tetraphenyl pyrrolone, 77
Thebacodeine, 152
Thiazole, 106
Thiocarbaminoglycolic acid, 152
Thiophene, 123
  as solvent, 125
Thiosaccharin, 112
Thiotoluidine, 30, 31
Thiotolyl urea, 124
Thioxanthone, 155
Toluene as solvent, 9, 125
Toluenesulfonate, 85
Toluidine, 121, 125
  as solvent, 107
Tolyl sulfonic chloride, 16
Tolylurea, 153
Triammonium citrate, 48
Trianiline arsine hydrochloride, 120
Trichloroethylene as solvent, 135
Trichlorotriphenyl carbinol, 117
Trimethyl stannane, 33

Trinaphthylene benzene, *see* Dekacyclene
Trinaphthyl carbinol, 18
Trinitrotoluene, 23, 28
Triphenyl arsine, 100
Triphenylbutane, 149
Triphenyl carbinol, 17
Triphenylethylene, 17
Triphenylguanidine, 9
Triphenylmethane, 17, 124, 125
Triphenylmethyl, 104, 116, 136
Triphenyl propane, 149
  pyrylium chloride, 92
Triquinylmethane, 115
Tropine, 124
Tungsten, 131
Turkey-red oil, 23, 24
Turpentine as solvent, 128
Tyrosine, 49

Urea, 99
Urethanes, 118
Uric acid, 96

Valeric aldehyde, *see* Amylal
Vanillin, 85
Veratrin, 156
Vinyl alcohol, 85
Volatile oils, 48
Vulcanization accelerators, 121

Water as solvent, 21
  in alcohols, estimation of, 67
Waxes, saponification of, 117
Wurtz reaction, 119

Xylene as solvent, 9, 126

Young's method, 66

Zein, 7
Zinc-copper couple, 140
Zinc diethyl, 140

LITERATURE OF THE CHEMICAL INDUSTRIES

On our shelves is the most complete stock of technical, industrial, engineering and scientific books in the United States. The technical literature of every trade is well represented, as is also the literature relating to the various sciences, including books useful for reference as well as those fitted for students' use as textbooks.

A large number of these we publish and for an ever increasing number we are the sole agents.

ALL INQUIRIES MADE OF US ARE CHEERFULLY AND CAREFULLY ANSWERED AND COMPLETE CATALOGS AS WELL AS SPECIAL LISTS SENT FREE ON REQUEST

D. VAN NOSTRAND COMPANY
Publishers and Booksellers
8 WARREN STREET NEW YORK

541.346

541.346 M11

a39001 0069979966

541 346 M11
MACARDLE D W THE USE OF SOLVENTS IN S

INSERT BOOK
MASTER CARD
FACE UP IN
FRONT SLOT
OF S.R. PUNCH

MASTER CARD

GLOBE 901144-0

UNIVERSITY OF ARIZ
LIBRARY